Поражение ткани почек при системной красной волчанке

Национальный Центр
Клинической Морфологической
Диагностики

Санкт-Петербург

Воробьева О.А.

Клинический диагноз СКВ

I. Световая микроскопия → *Гистологический рисунок*
Основа(!) дальнейших диагностических рассуждений

Первичный дифференциально-диагностический ряд

II. Иммунофлюоресценция / Иммуногистохимия
Состав и локализация повреждающего агента
Механизм повреждения → терапевтический подход

ГИСТОЛОГИЧЕСКОЕ ЗАКЛЮЧЕНИЕ (I & II)

Терапевтическое решение

III. Электронная микроскопия
Ультраструктура
- Уточнение/дополнение к установленному диагнозу
- Случайные находки

ГИСТОЛОГИЧЕСКОЕ ЗАКЛЮЧЕНИЕ (I & II & III)

***СКВ – частое вовлечение ткани почек*:**

- **Все компартменты ткани почки**
- **Широкая вариабельность гистологической картины**
- **Неоднородность повреждения**
- **Трансформация изменений с течением времени**
- **Нефробиопсия → «почечный» диагноз, динамика, *прогноз, терапия***

Lupus-нефрит:
Развивается в ≈60% случаев СКВ
Из них, ≈10%-20% прогрессируют в тХПН

Lupus-нефрит (2004):

I. Минимальный
II. Мезангиопролиферативный
III. Фокальный (A/C)
IV. Диффузный (A/C; G/S)
V. Мембранозный (V; V+III; V+IV)
VI. Склерозирующий

Пересмотр классификации Lupus-нефрита 2018

- ✓ *Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in SLE revisited. J Am Soc Nephrol. 2004; 15: 241–250.*
- ✓ *D'Agati VD, Stokes MB. Renal disease in SLE, MCTD, Sjogren's syndrome, and RA. In Jennette JC et al.: Heptinstall's Path of the kidney. 7th ed. 2014; 560-610.*

www.kidney-international.org

meeting report

Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices

Ingeborg M. Bajema[1], Suzanne Wilhelmus[1], Charles E. Alpers[2], Jan A. Bruijn[1], Robert B. Colvin[3], H. Terence Cook[4], Vivette D. D'Agati[5], Franco Ferrario[6], Mark Haas[7], J. Charles Jennette[8], Kensuke Joh[9], Cynthia C. Nast[7], Laure-Hélène Noël[10], Emilie C. Rijnink[1], Ian S.D. Roberts[11], Surya V. Seshan[12], Sanjeev Sethi[13] and Agnes B. Fogo[14]

Kidney International (2018) ■, ■–■; https://doi.org/10.1016/j.kint.2017.11.023

Revision c Nephrolog for lupus modified chronicity

Ingeborg M. Ba
H. Terence Coo
Cynthia C. Nast
Sanjeev Sethi[13]

Colvin[3],
, Kensuke Joh[9],
shan[12],

Table 1 | Phase 1 recommendations for lupus nephritis classification

Category	Recommendation	Comments on ISN/RPS guidelines
Class II	Definition for mesangial hypercellularity adjusted: Four or more nuclei fully surrounded by matrix in the mesangial area not including the hilar region (A)	Cuttoff for mesangial hypercellularity unclear
Class III and IV	The term endocapillary proliferation is replaced by endocapillary hypercellularity (B)	Definition for endocapillary proliferation unclear; the term proliferation was considered imprecise
	The term crescent is used for a lesion consisting of extracapillary hypercellularity, composed of a variable mixture of cells. Fibrin and fibrous matrix may be present; 10% or more of the circumference of Bowman's capsule should be involved.	Extracapillary proliferation involving > 25% of the circumference of Bowman's capsule was original cutoff. There were no definitions for fibrous or fibrocellular crescents
	Cellular crescent: more than 75% cells and fibrin and less than 25% fibrous matrix (C)	
	Fibrous crescent: more than 75% fibrous matrix and less than 25% cells and fibrin (D)	
	Fibrocellular crescent: 25%–75% cells and fibrin and the remainder fibrous matrix (E)	
	Adhesion: an area of isolated continuity of extracellular matrix material between the tuft and capsule even when the underlying segment does not have overt sclerosis (F)	There was no definition for an adhesion
	Fibrinoid necrosis: fibrin associated with glomerular basement membrane disruption and/or lysis of the mesangial matrix; this lesion does not require the presence of karyorrhexis	There was no definition for fibrinoid necrosis
	Elimination of segmental and global subdivions of class IV	Definitions for segmental and global were unclear; interobserver variability was large; clinical significance uncertain
	Modification of the NIH lupus nephritis activity and chronicity scoring system (Table 2) to be used instead of the currently used A, C, and A/C parameters	Designation of activity/chronicity through A, C, and A/C considered too broad and nonspecific; preference for a semiquantitative approach to describe active and chronic lesions
Tubulointerstitial lesions	Indicate whether interstitial inflammation occurs in presence or absence of interstitial fibrosis	Lack of cut-off values for reporting the severity of tubulointerstitial lesions

■–■; https://doi.org/10.1016/

Table 1 | Phase 1 recommendations for lupus nephritis classification

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Class III and IV	The term endocapillary proliferation is replaced by endocapillary	Definition for endocapillary proliferation unclear; the term
	Modification of the NIH lupus nephritis activity and chronicity scoring system (Table 2) to be used instead of the currently used A, C, and A/C parameters	Designation of activity/chronicity through A, C, and A/C considered too broad and nonspecific; preference for a semiquantitative approach to describe active and chronic lesions
Tubulointerstitial lesions	Indicate whether interstitial inflammation occurs in presence or absence of interstitial fibrosis	Lack of cut-off values for reporting the severity of tubulointerstitial lesions

Table 2 | Proposed modified NIH lupus nephritis activity and chronicity scoring system

Modified NIH activity index	Definition	Score
Endocapillary hypercellularity	Endocapillary hypercellularity in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Neutrophils/karyorrhexis	Neutrophils and/or karyorrhexis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrinoid necrosis	Fibrinoid necrosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Hyaline deposits	Wire loop lesions and/or hyaline thrombi in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Cellular/fibrocellular crescents	Cellular and/or fibrocellular crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Interstitial Inflammation	Interstitial leukocytes in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		***0–24***
Modified NIH chronicity index	**Definition**	**Score**
Total glomerulosclerosis score	Global and/or segmental sclerosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrous crescents	Fibrous crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Tubular atrophy	Tubular atrophy in <25% (1+), 25%–50% (2+), or >50% (3+) of the cortical tubules	0–3
Interstitial fibrosis	Interstitial fibrosis in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		***0–12***

NIH, National Institutes of Health.

Sanjeev Sethi

■–■; https://doi.org/10.1016/

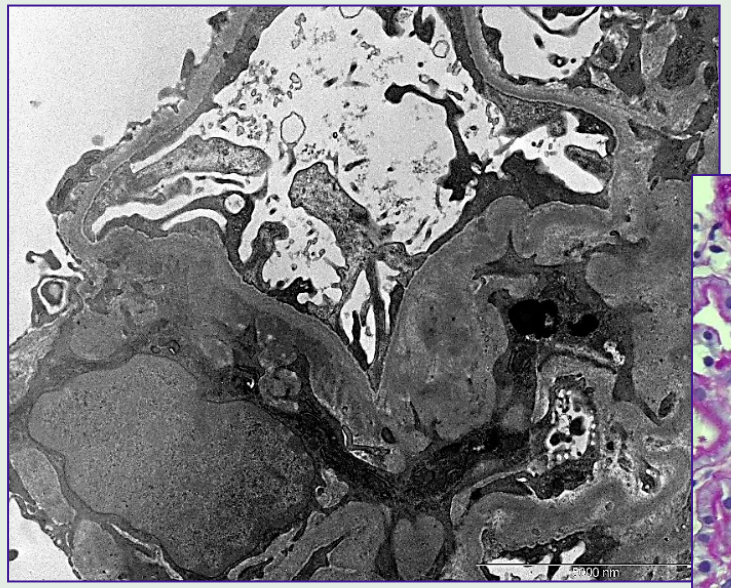
Пересмотр классификации Lupus-нефрита 2018

- Определены понятия «мезангиальная гиперклеточность» и «эндокапиллярная гиперклеточность»
- Определено понятие «полулуние» и его стадии (клеточное, фиброзно-клеточное, фиброзное)
- Определены и модифицированы понятия «фибриноидный некроз» и «адгезия»
- Ликвидировано подразделение IV класса на «сегментарный» и «глобальный» варианты
- Отмечена обязательность оценки тубуло-интерстициального воспаления, его тяжести и связи с тубуло-интерстициальным фиброзом
- Модифицирована система подсчета индексов активности и хронизации:

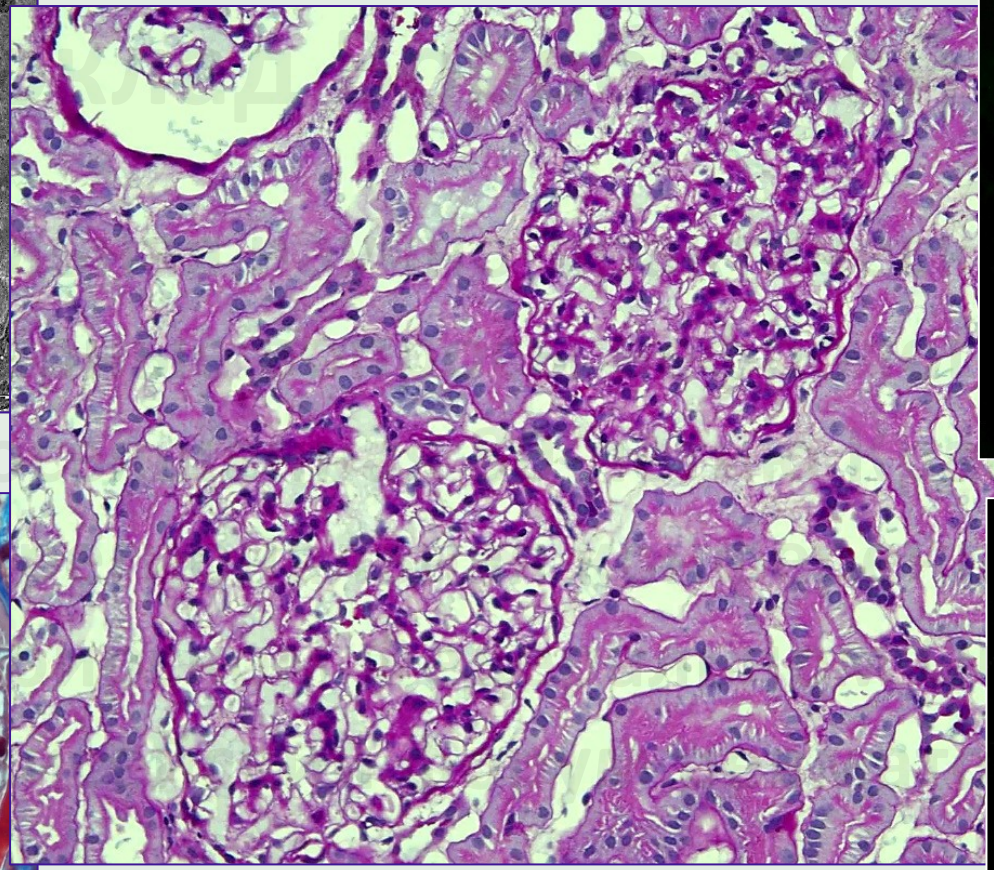
- Объективизирована бальная оценка
- Введены дополнительные признаки (кариорексис, фиброзно-клеточные полулуния)

✓ *Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the ISN/RPS classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. Kidney International. 2018; 93(4): 789-796.*

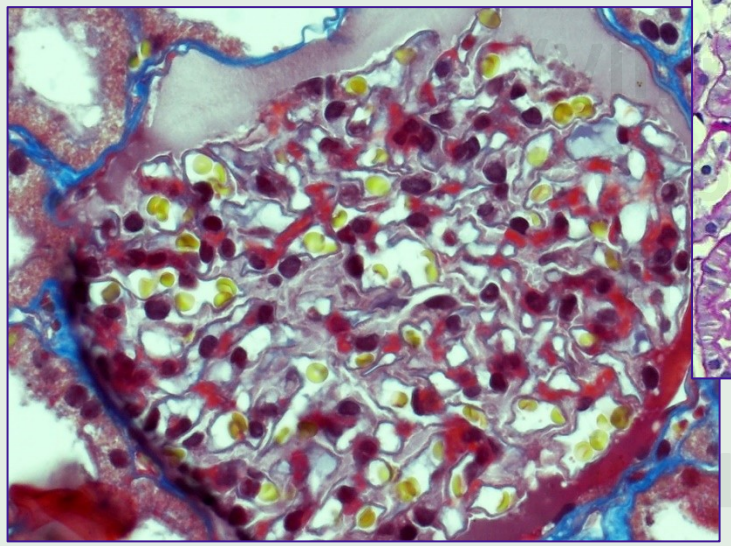
Класс I



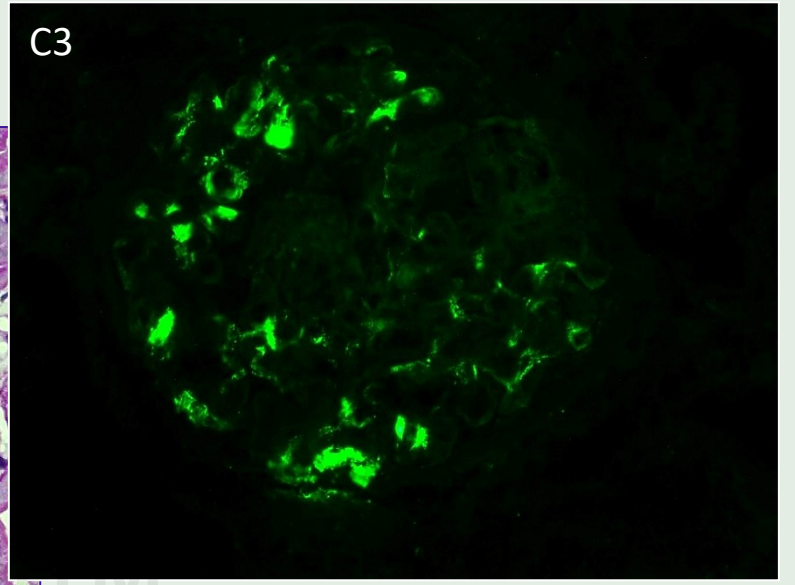
x5K

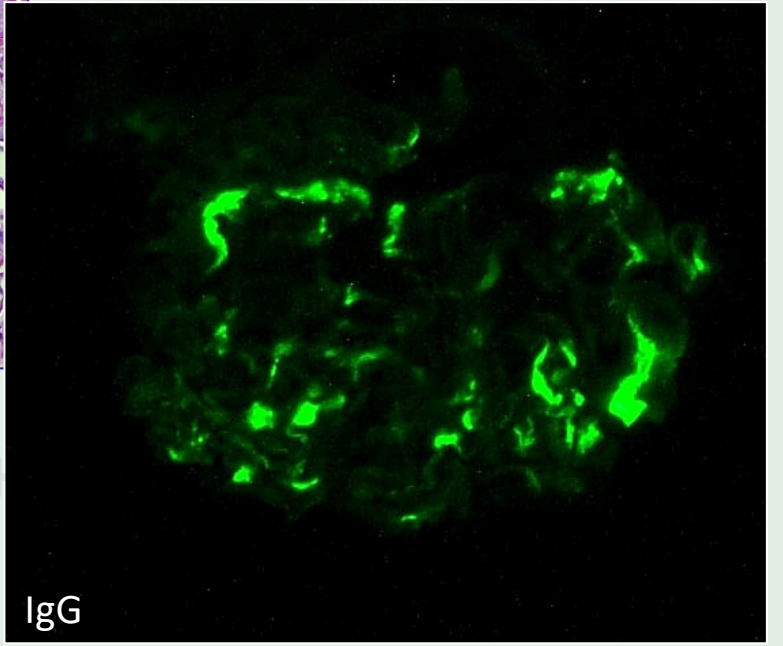


PAS, x200



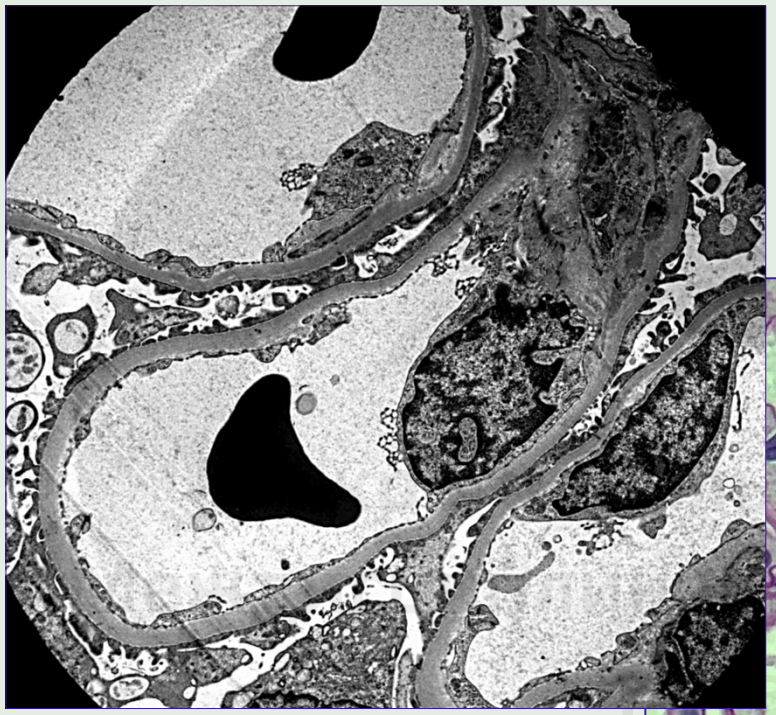
Masson’s, x200



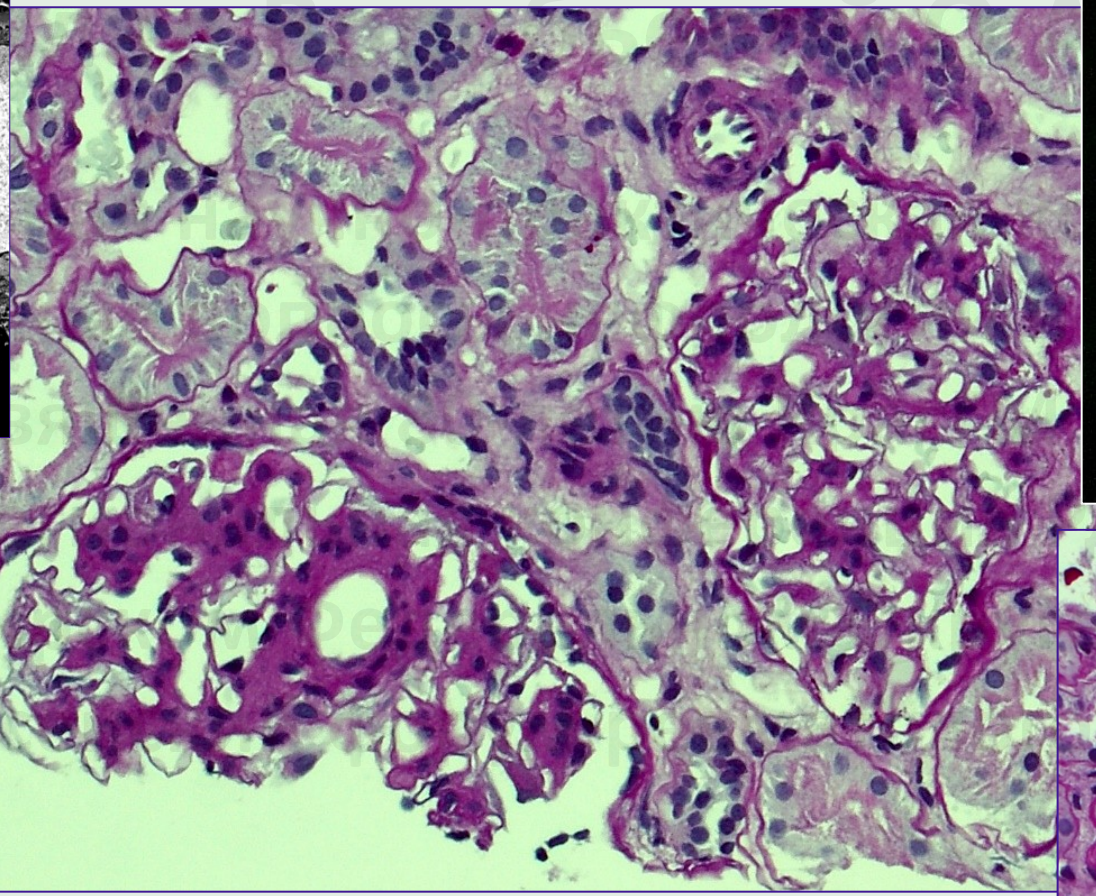


Из личного архива Воробьевой О.А., ООО «НЦКМД»

Класс II



х3К



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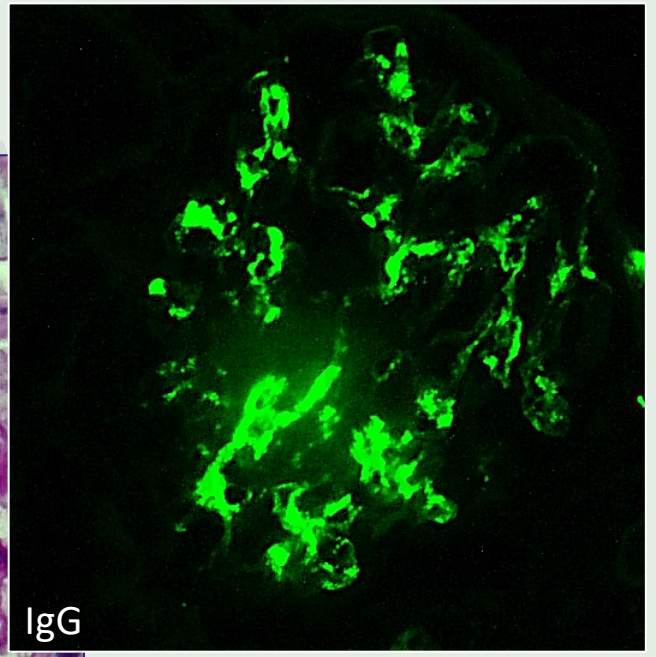
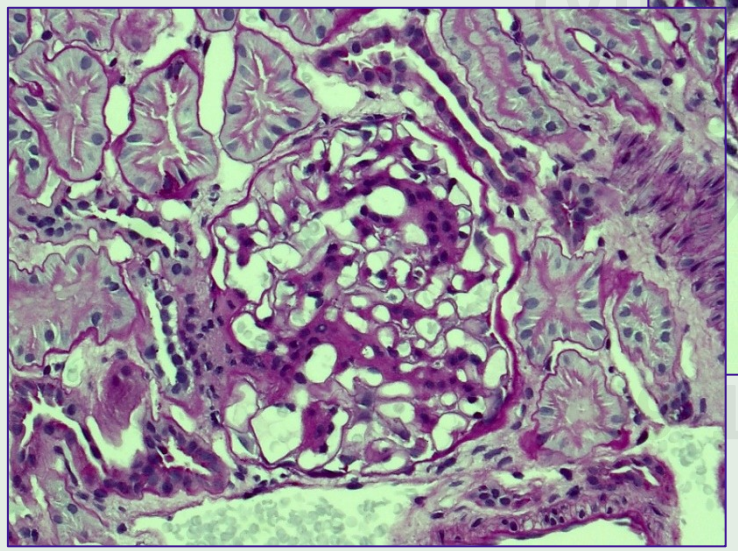
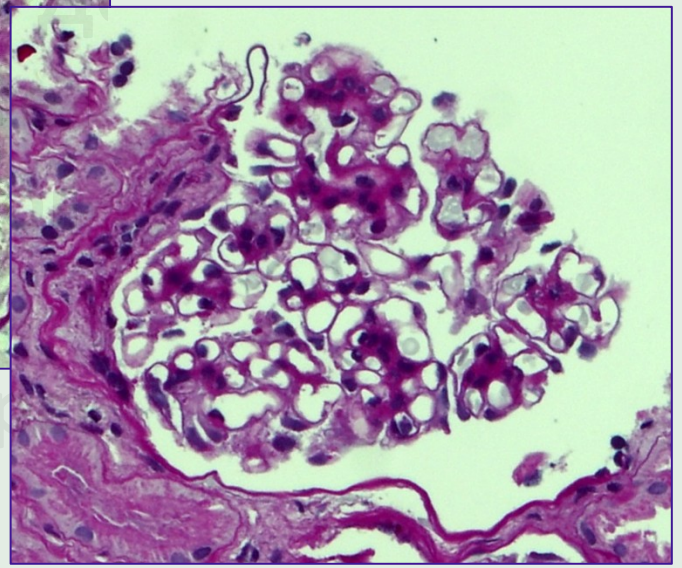


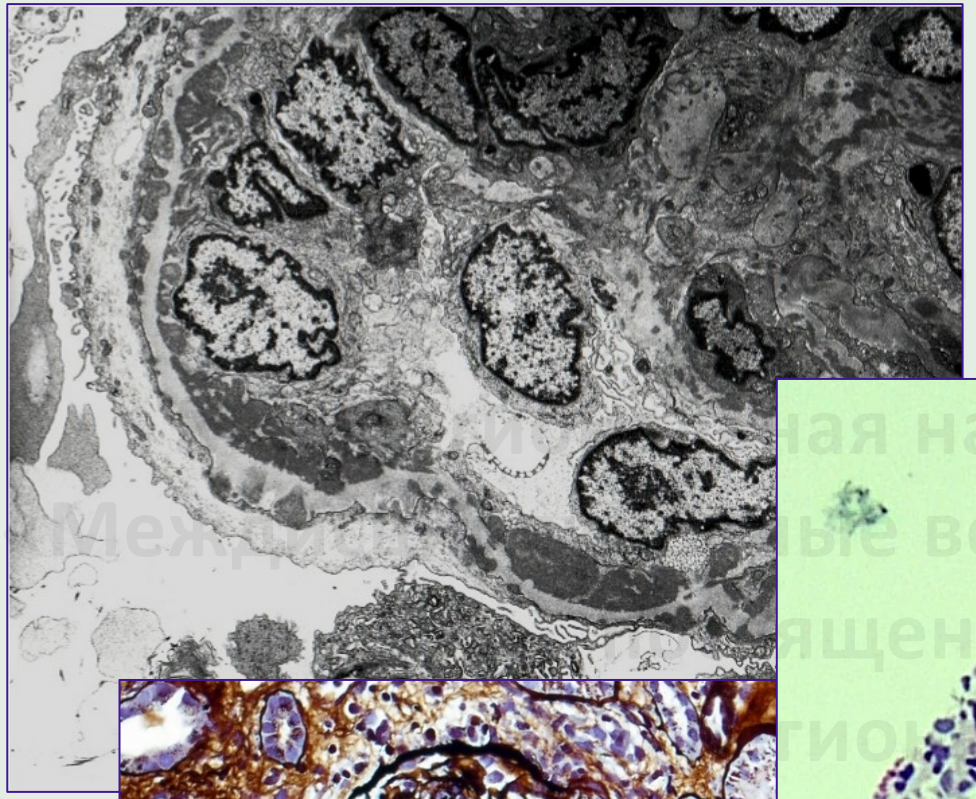
IgG



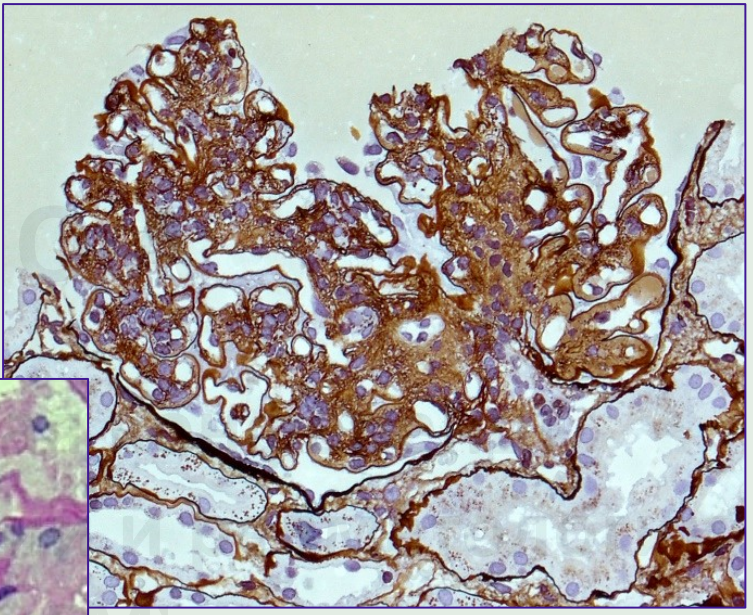


Из личного архива Воробьевой О.А., ООО «НЦКМД»

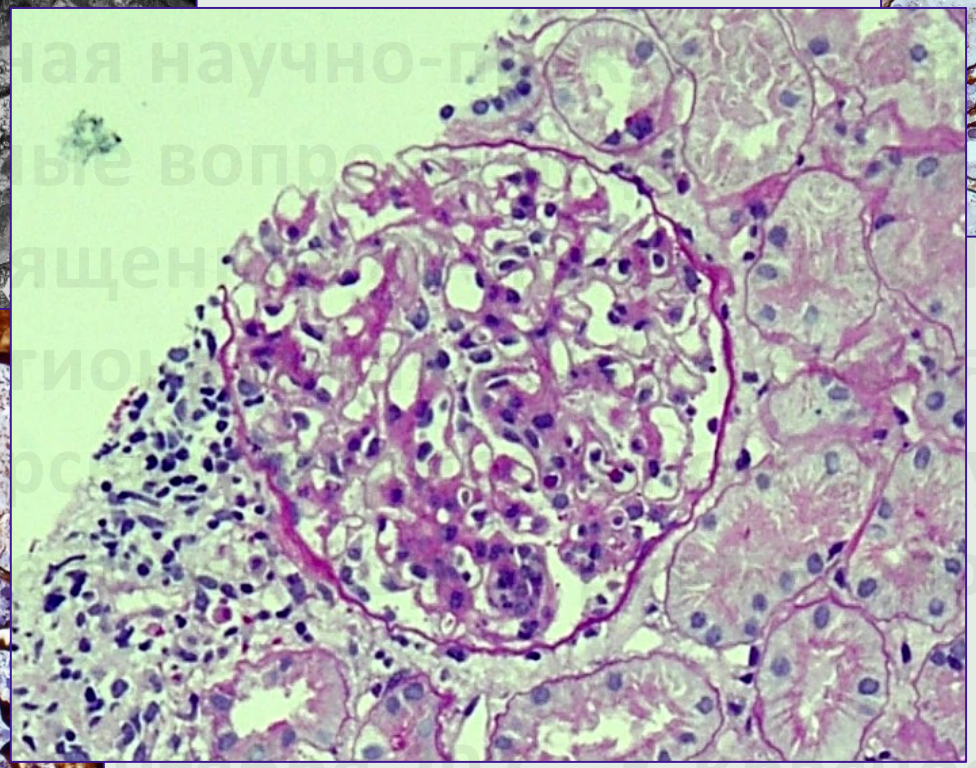
Класс III/IV



х3К



Jones’, x200



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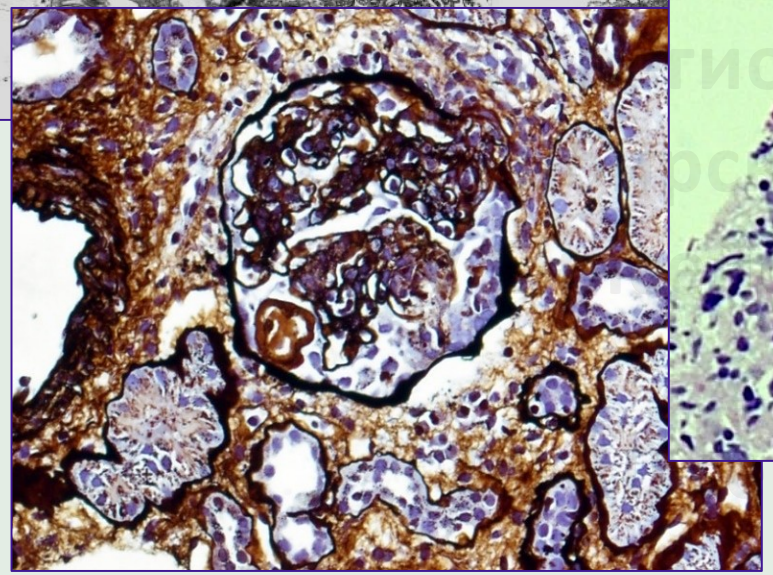
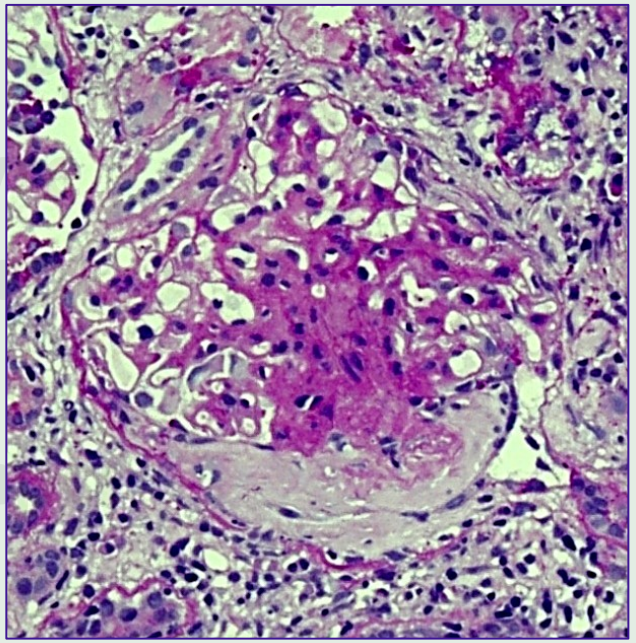
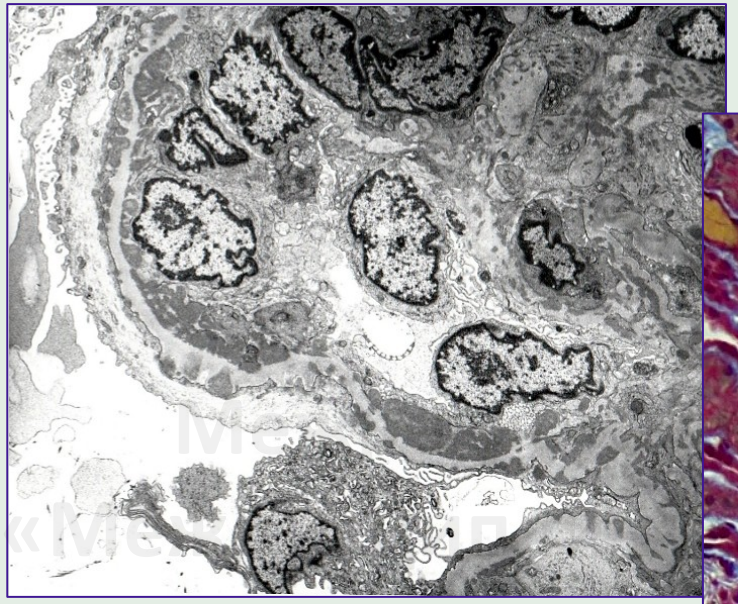


Jones’, x200

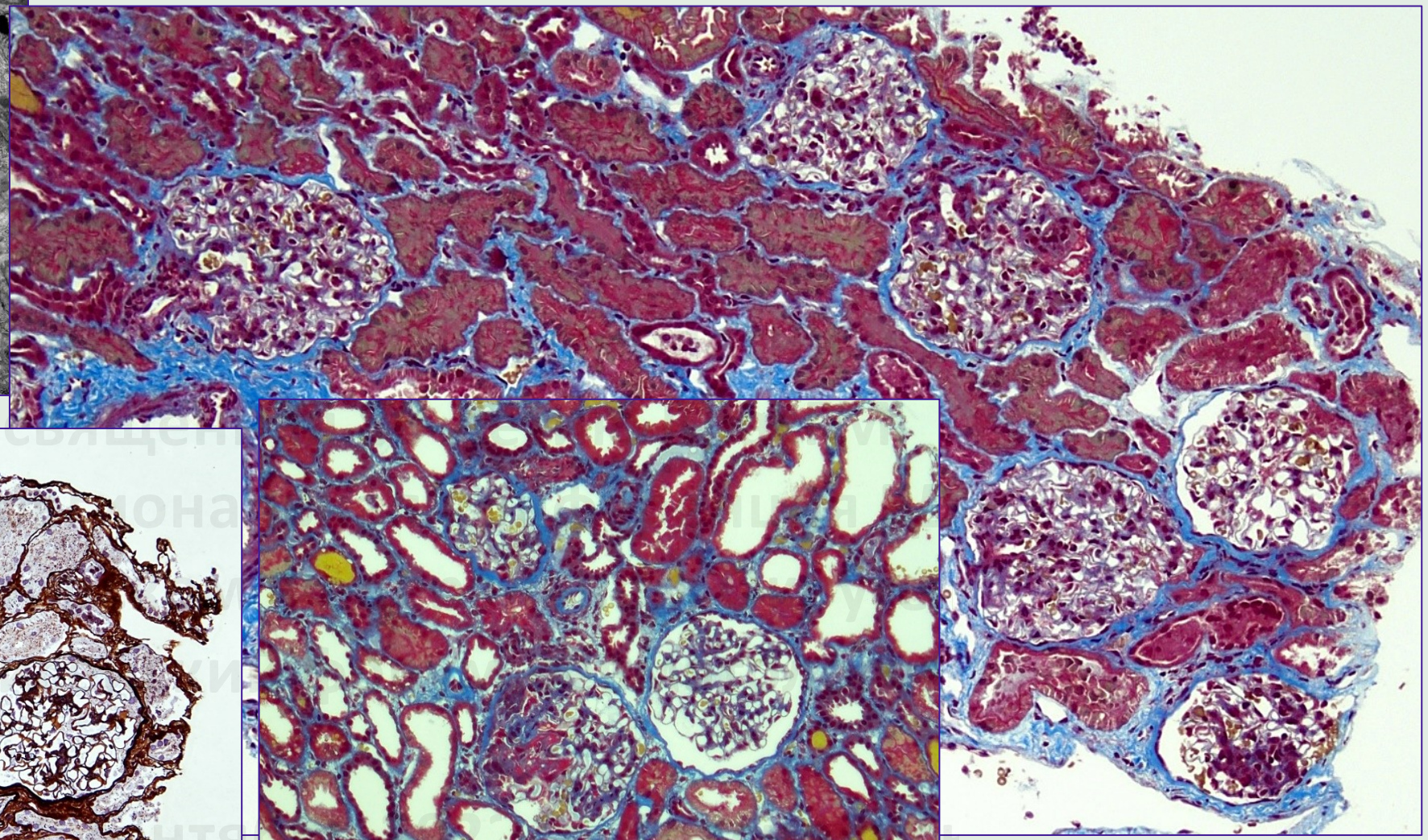


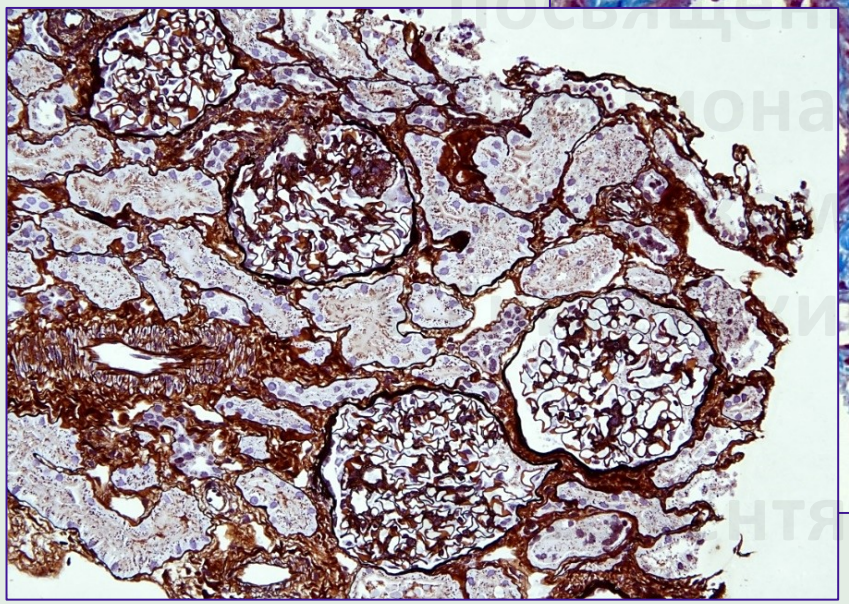
Из личного архива Воробьевой О.А., ООО «НЦКМД»

Класс III



х3К





Jones’, x100

Masson’s, x100

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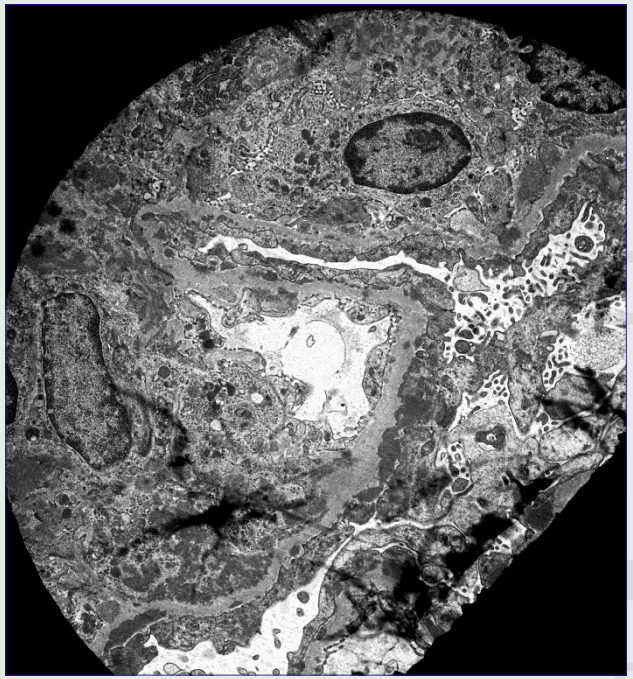
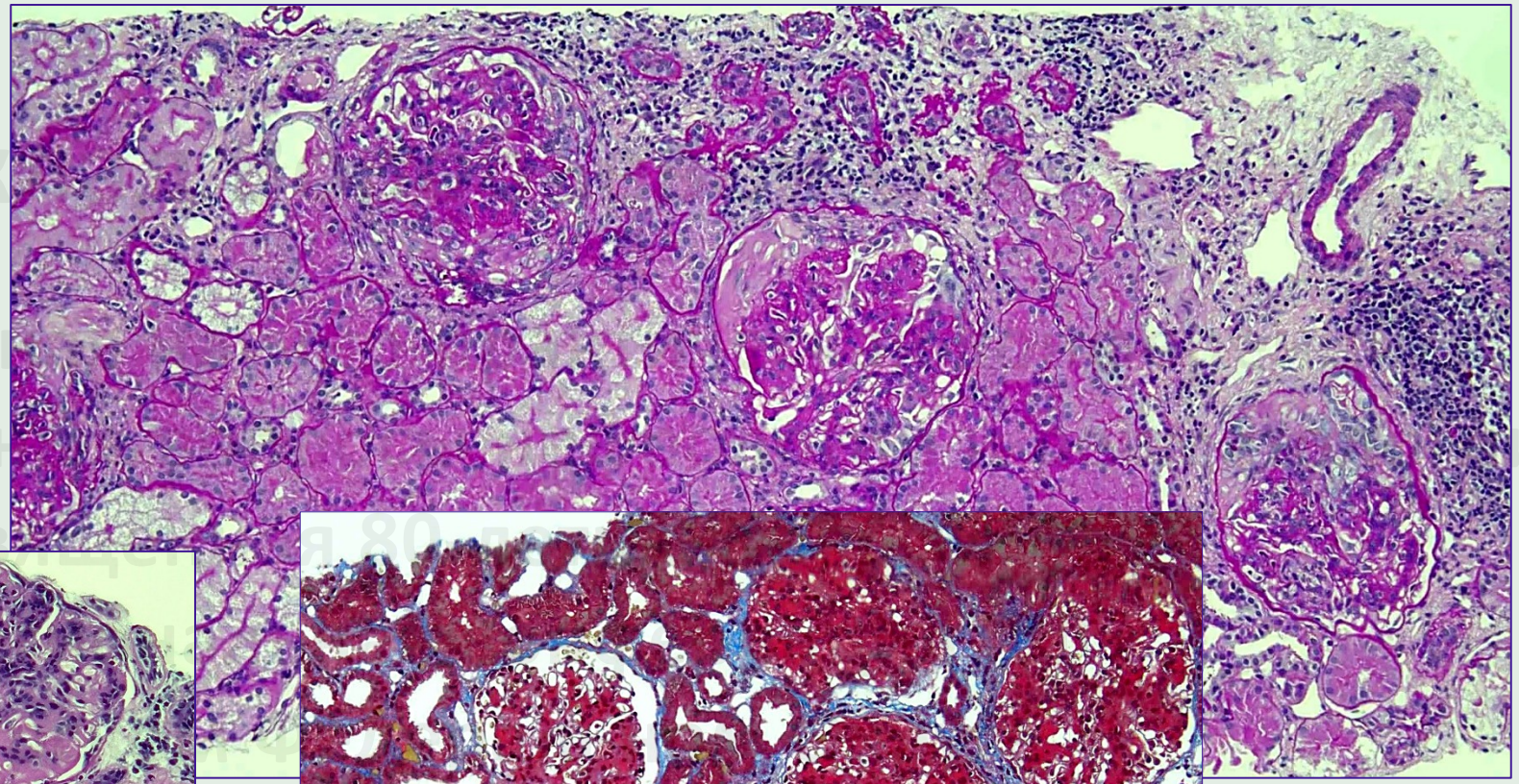
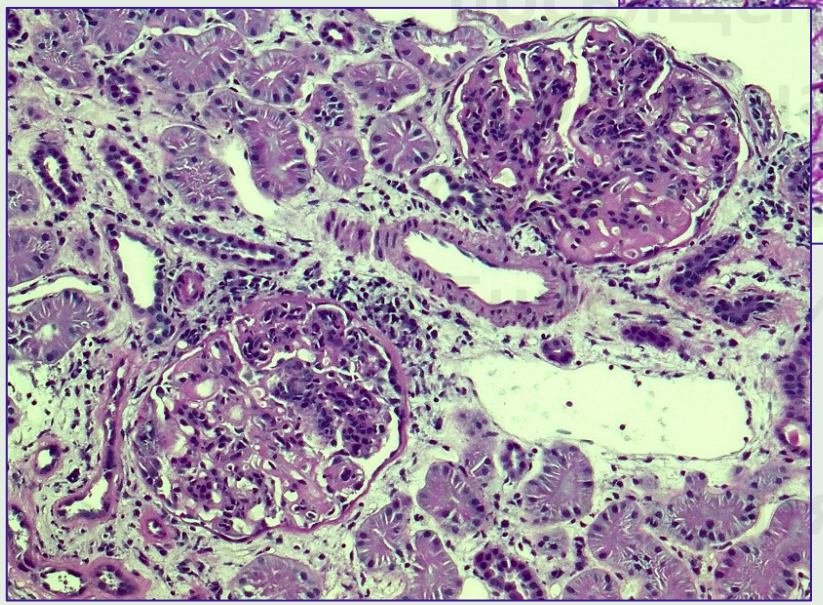
Класс IV



x1,2K



PAS, x100



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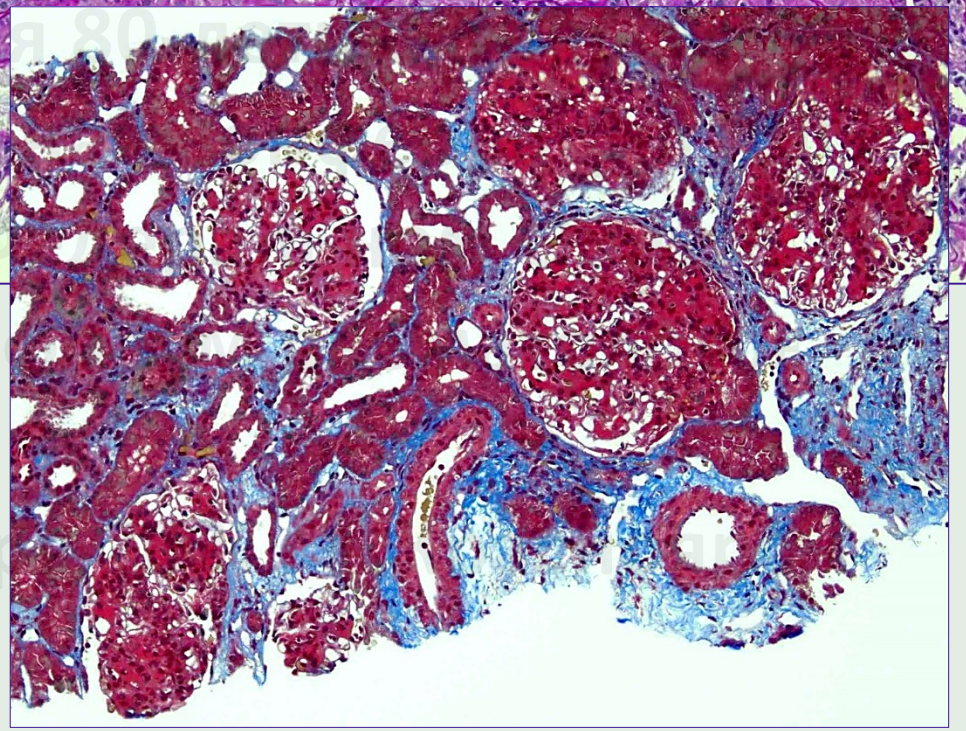
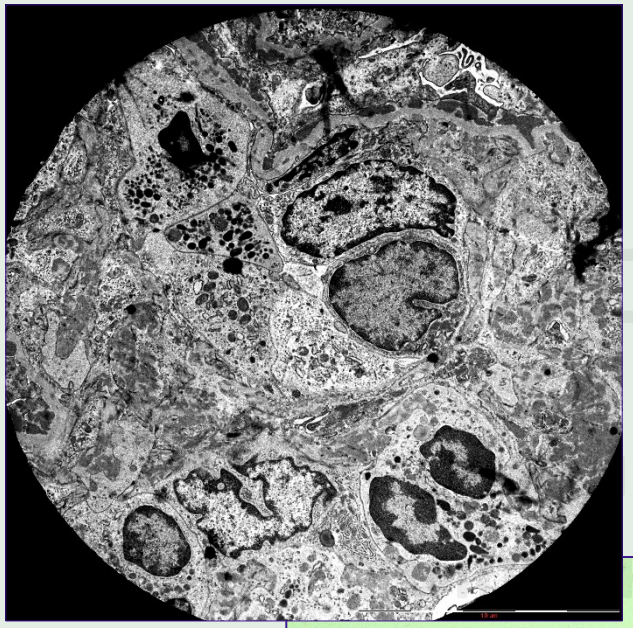


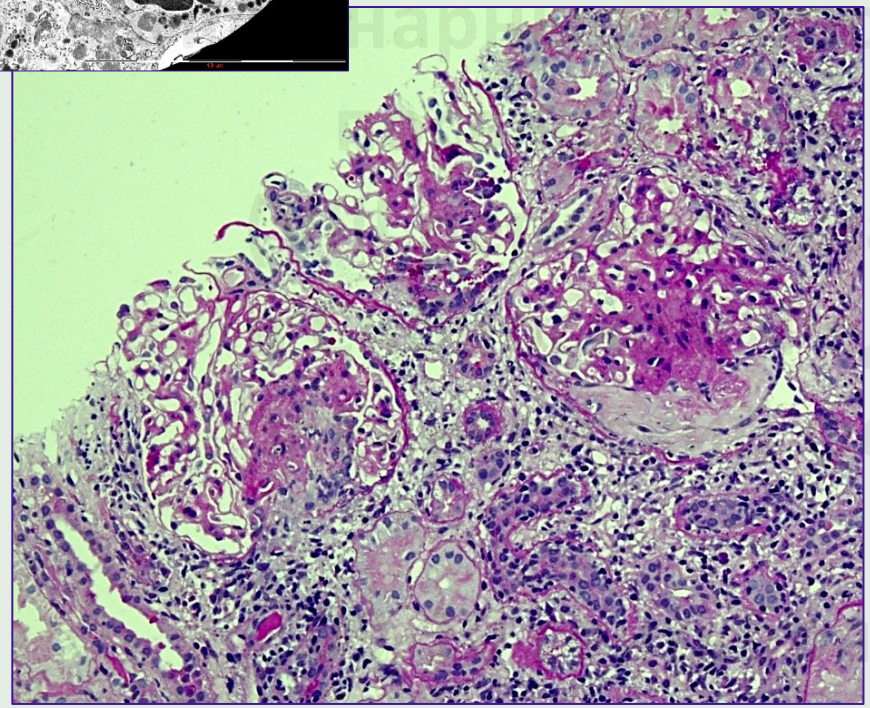
Masson’s, x100

Из личного архива Воробьевой О.А., ООО «НЦКМД»

Класс IV



х3К



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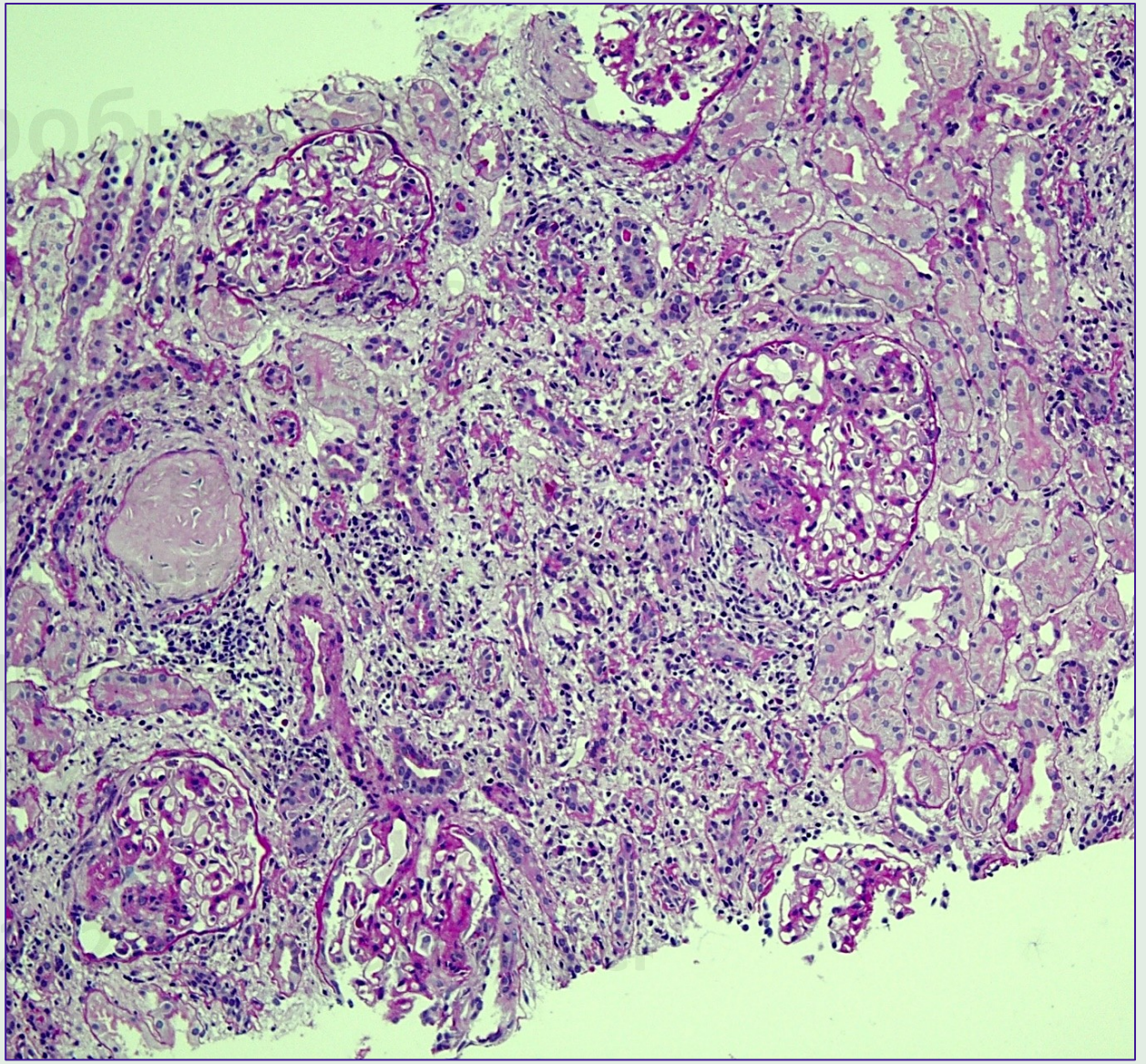
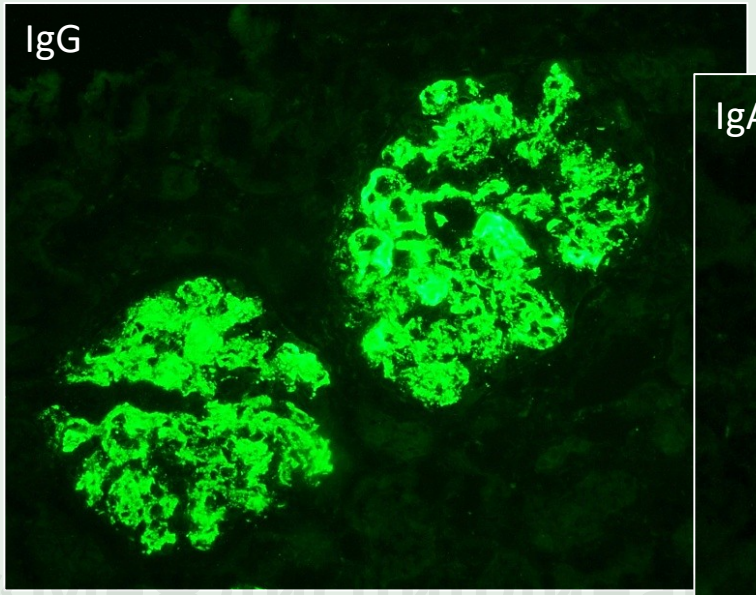
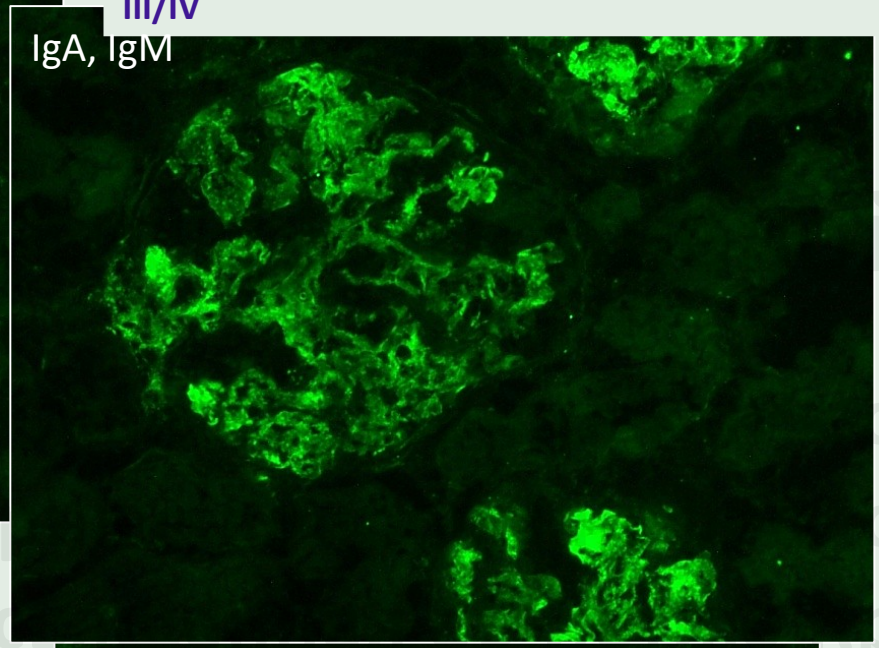


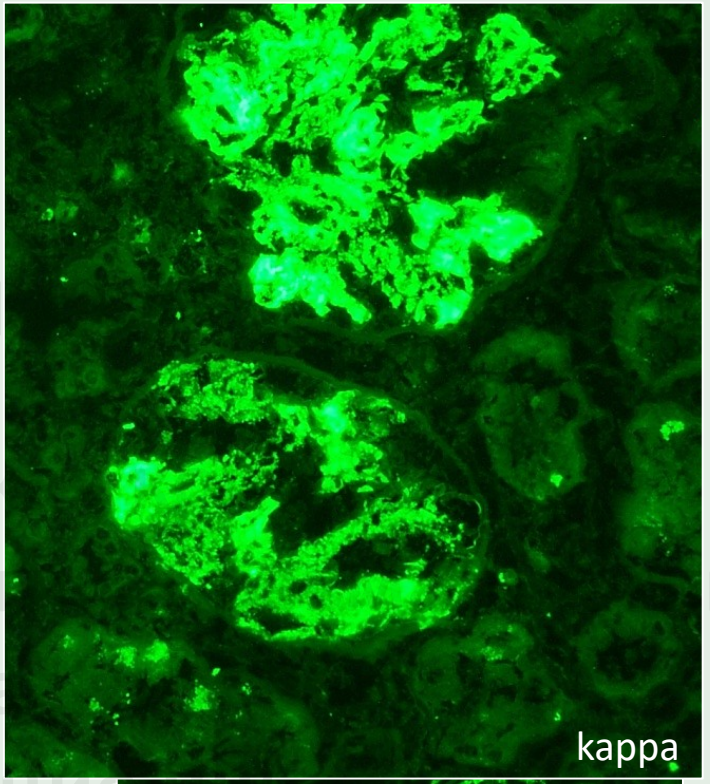
PAS, х100

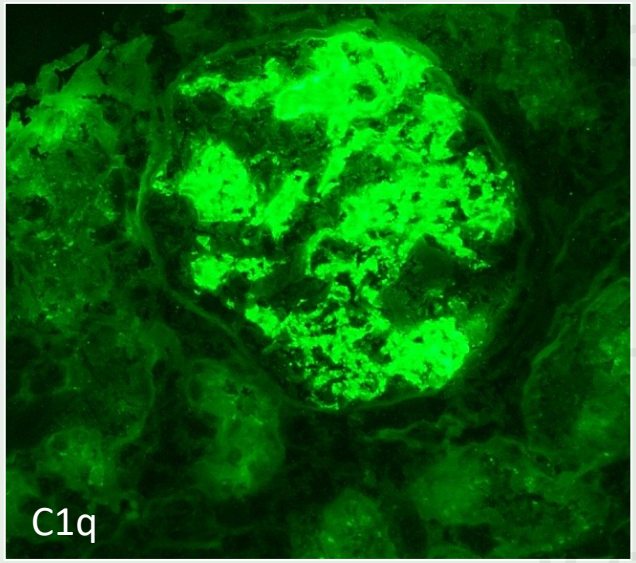
Из личного архива Воробьевой О.А., ООО «НЦКМД»

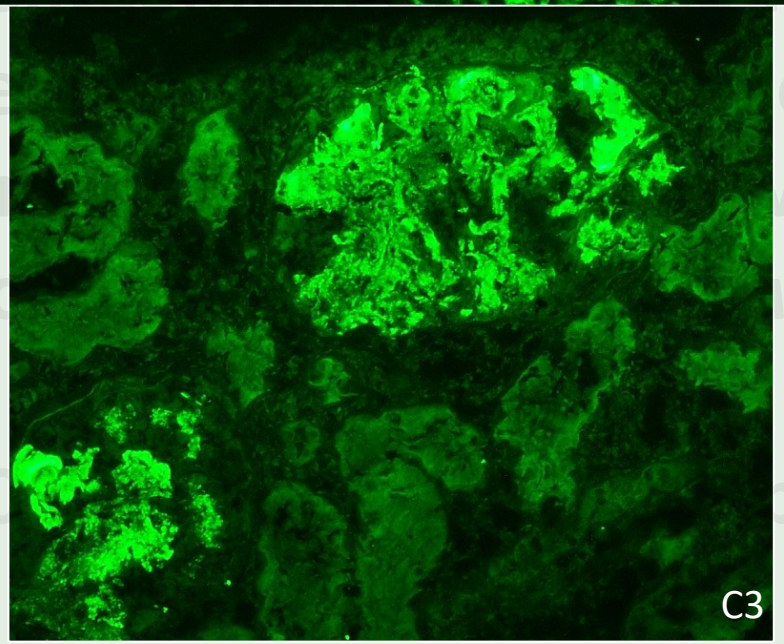
Иммунокомпозиция “full-house”, классы III/IV

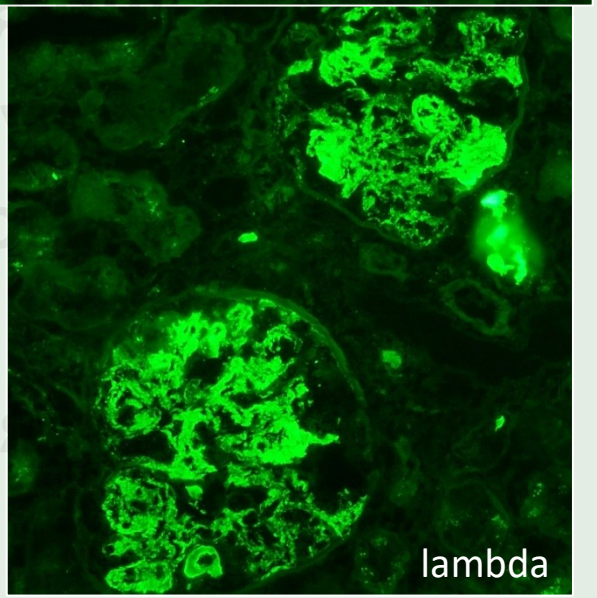








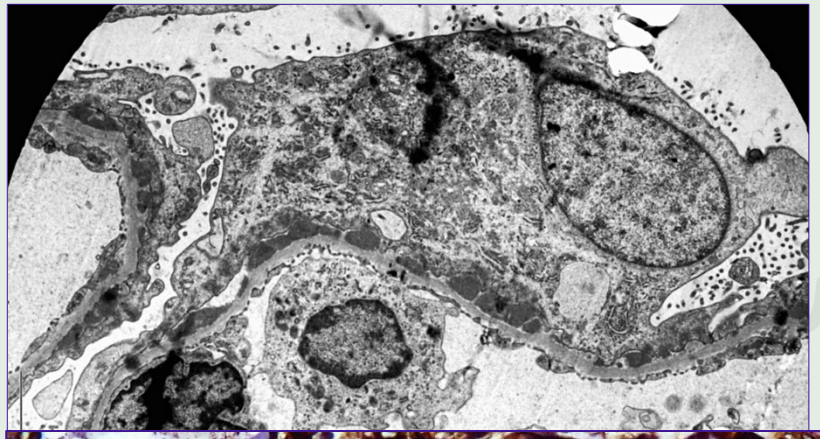


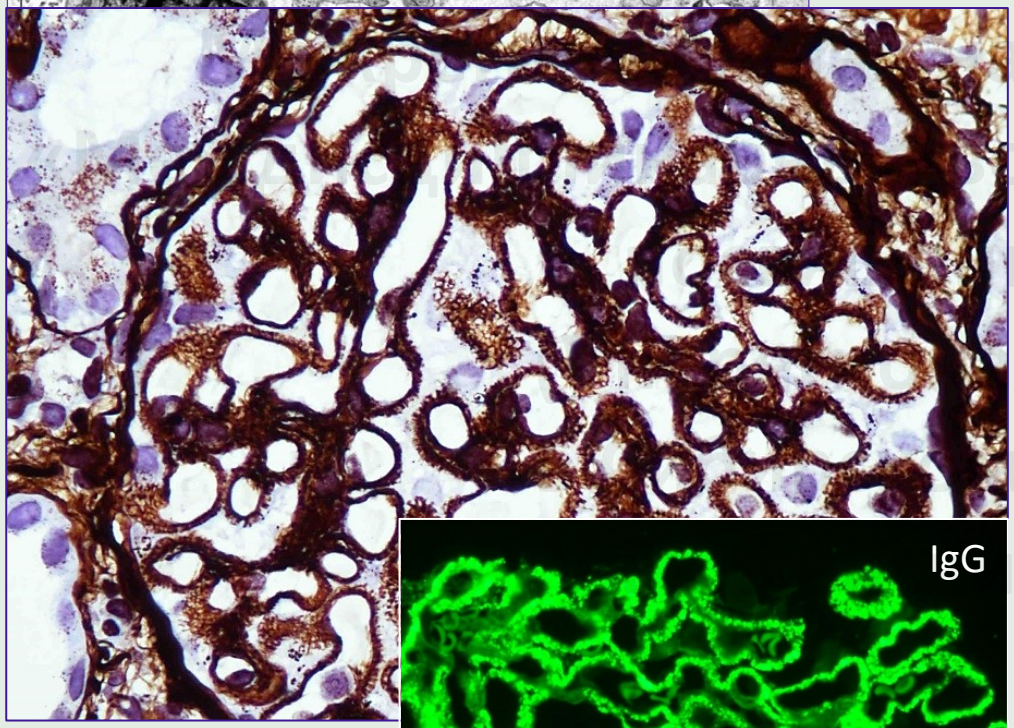


Из личного архива Воробьевой О.А., ООО «НЦКМД»

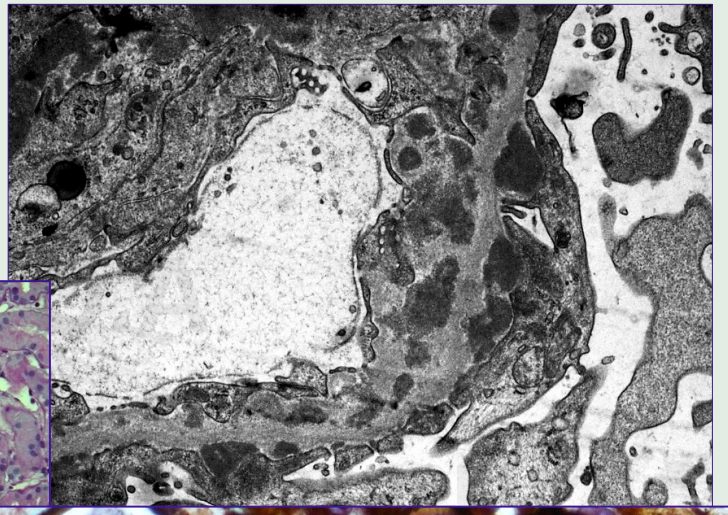
Класс V

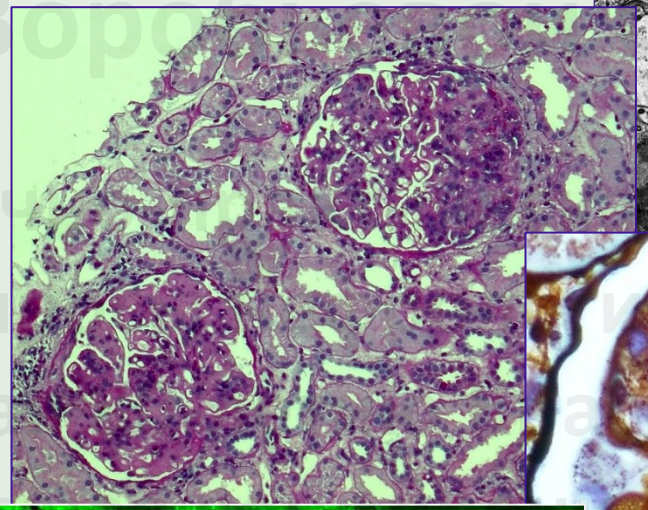
V или V+III/IV

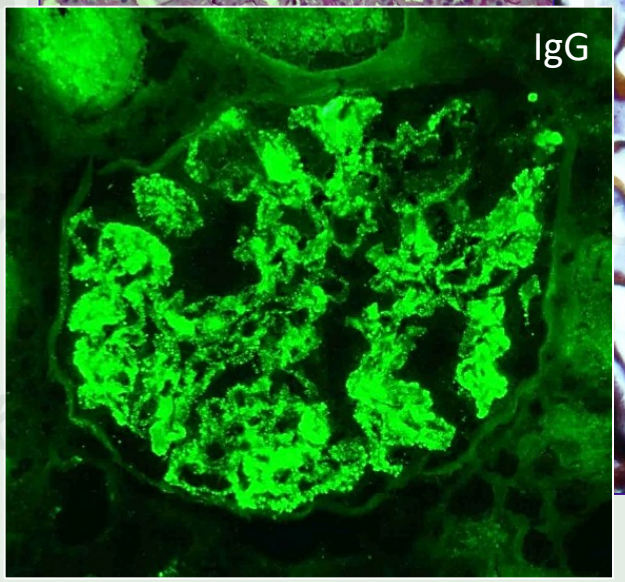


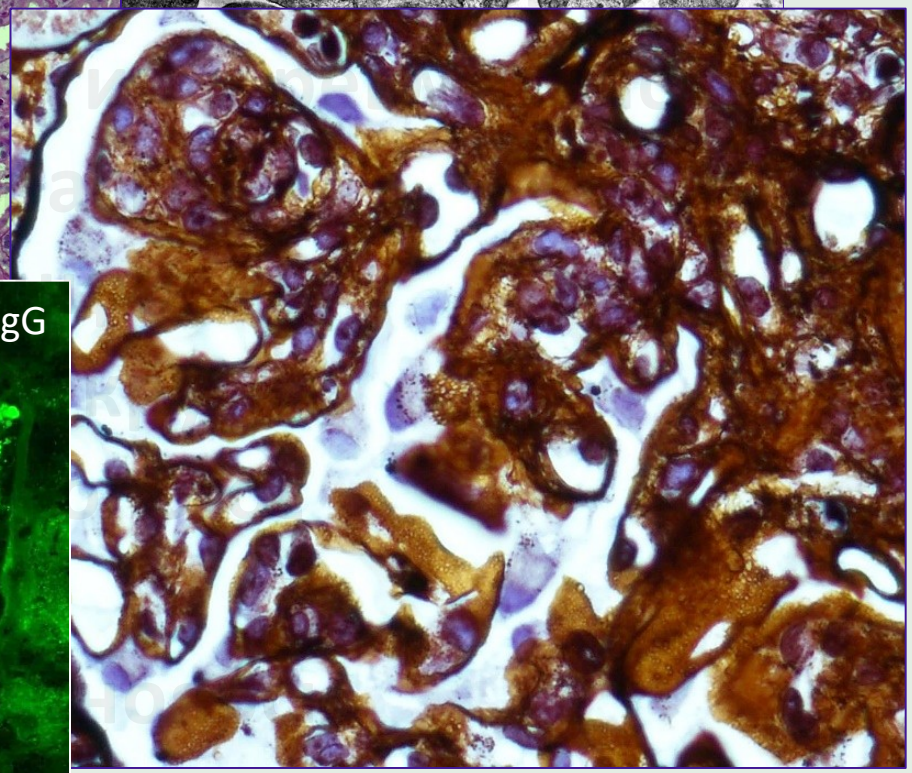


Класс V





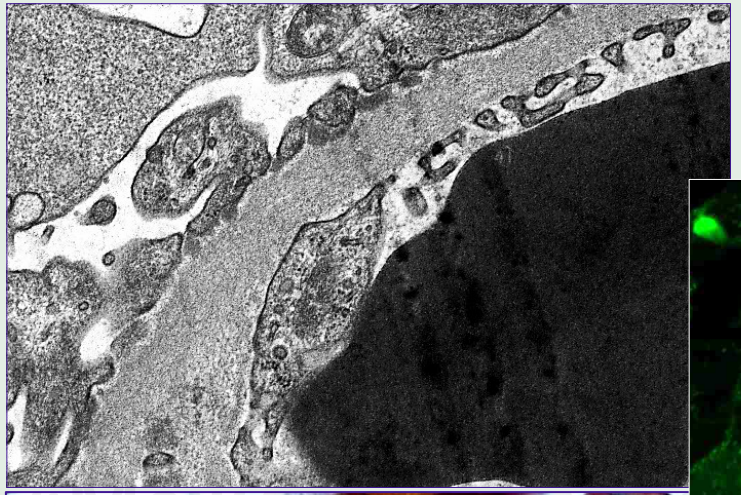


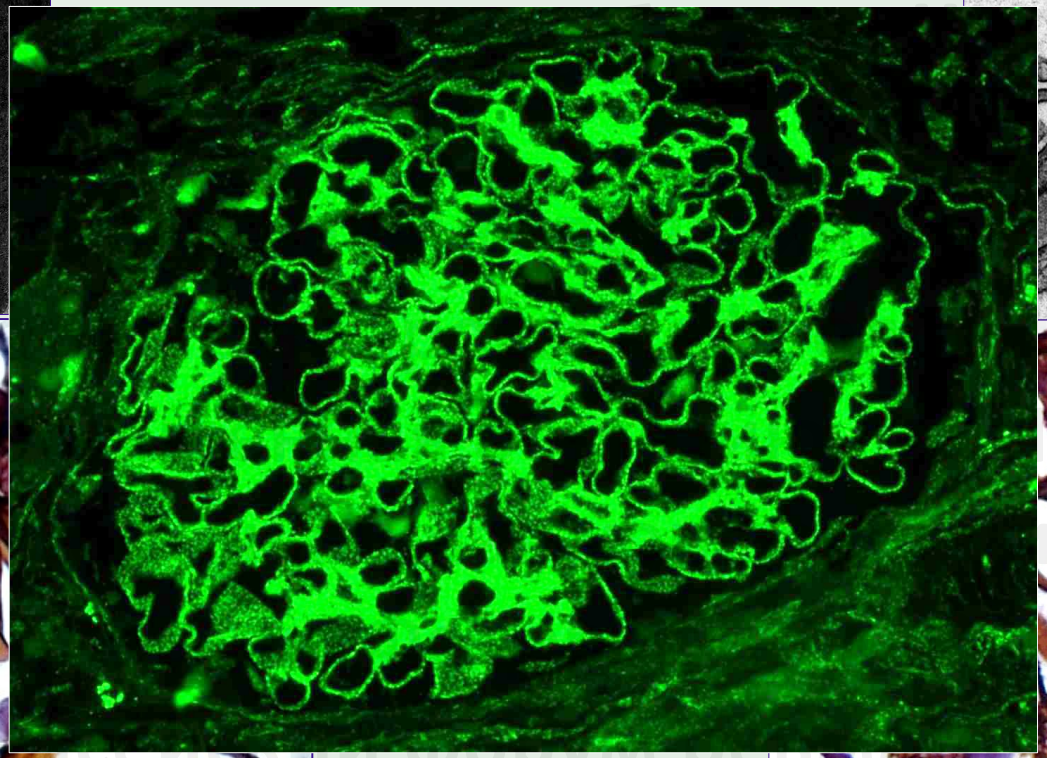


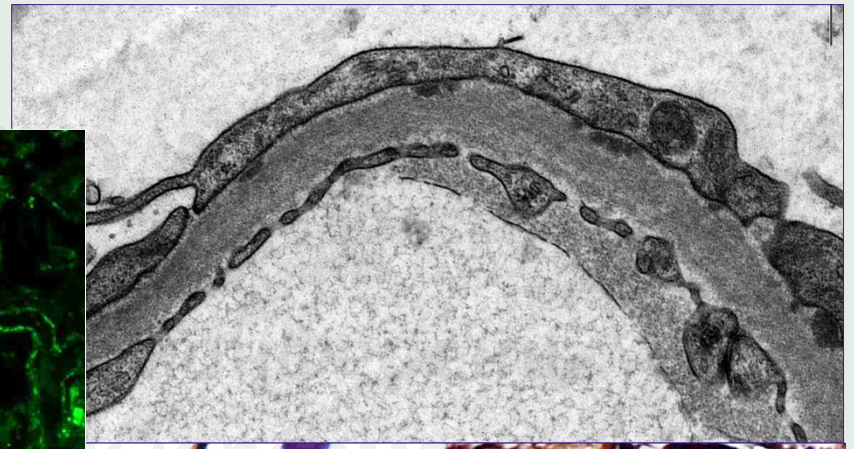
Класс V & III/IV

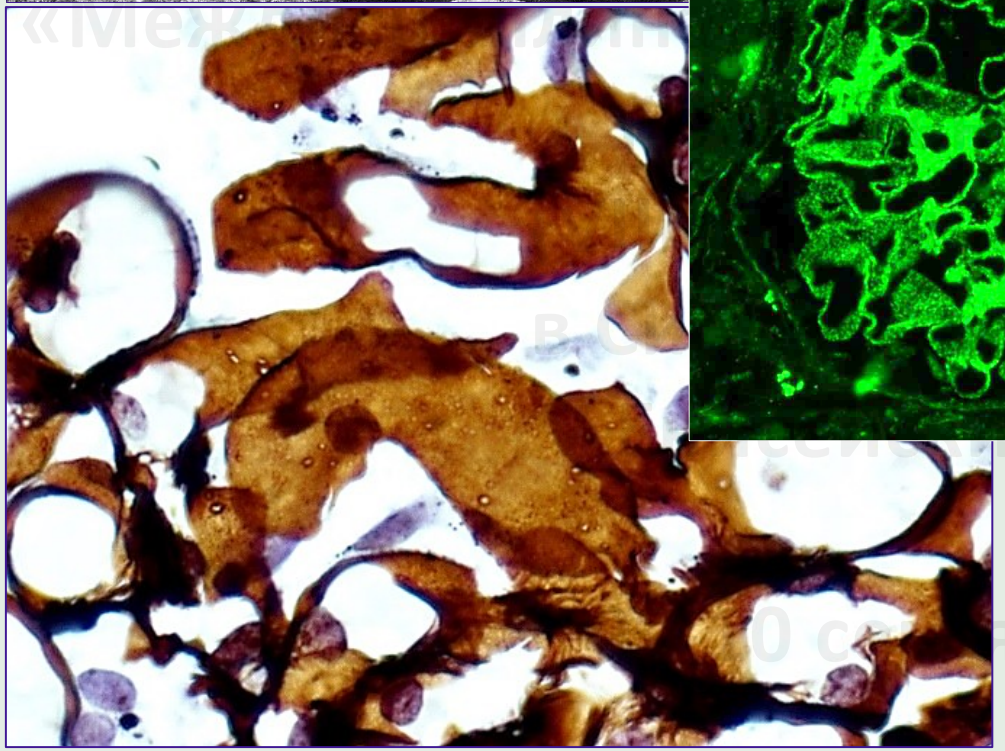
Из личного архива Воробьевой О.А., ООО «НЦКМД»

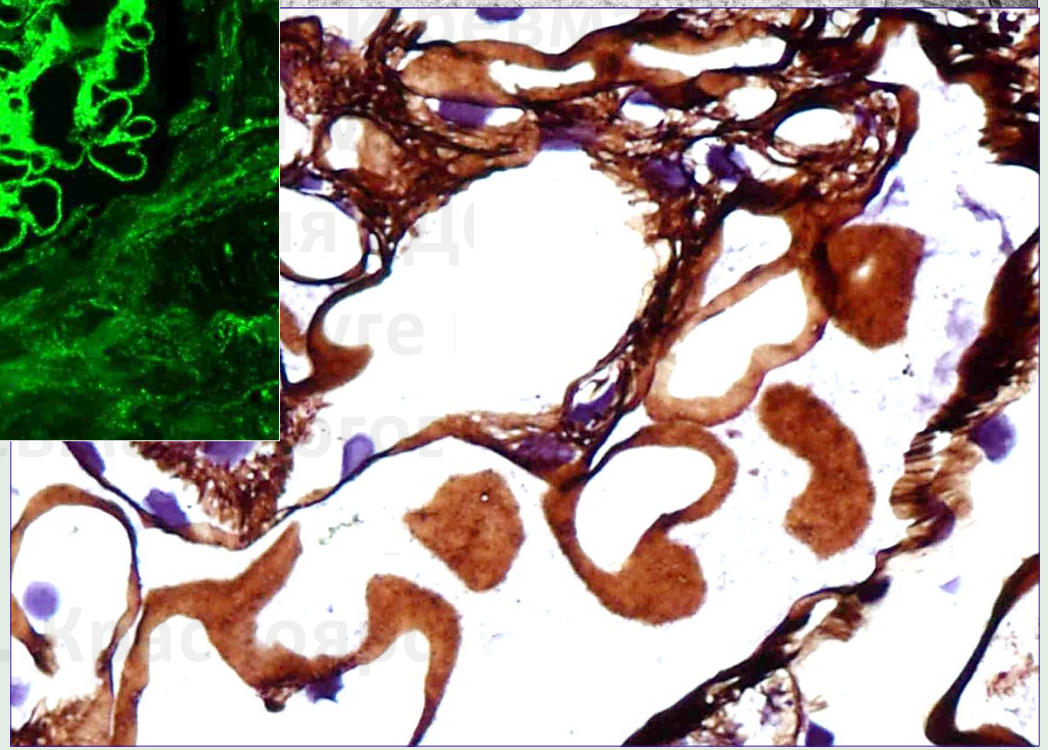
Класс V











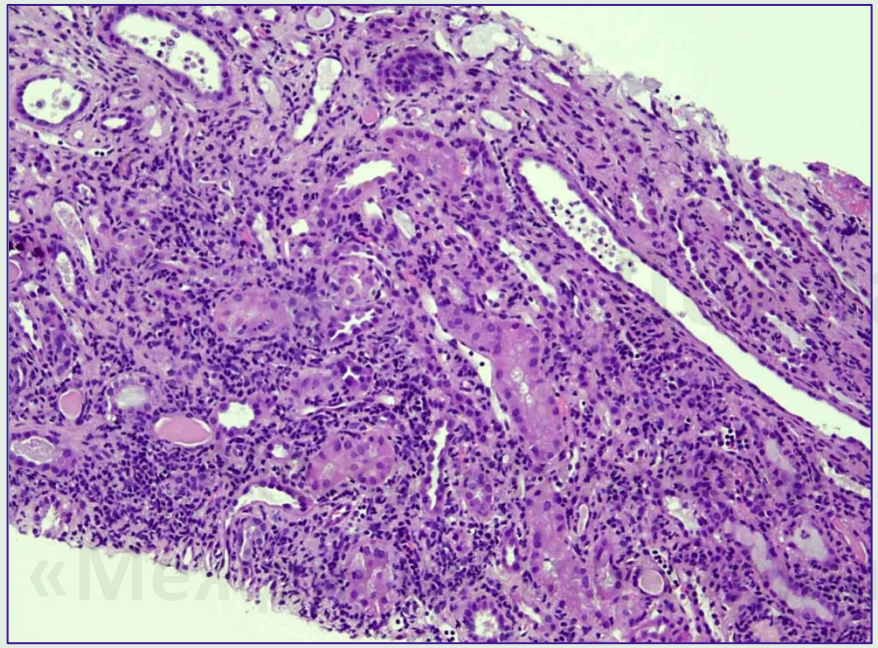
Из личного архива Воробьевой О.А., ООО «НЦКМД»

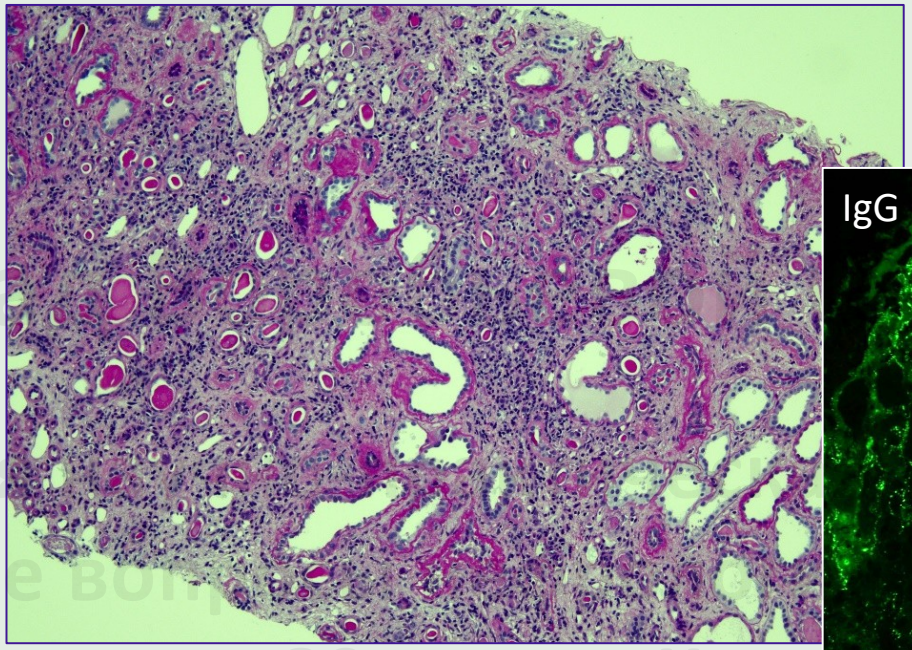
Тубуло-интерстициальное воспаление при Lupus-нефрите

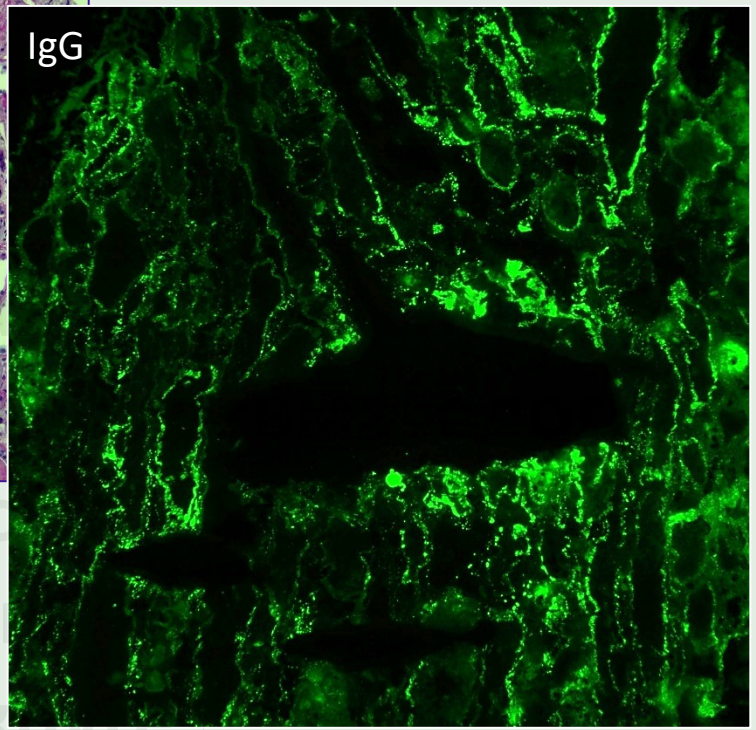
- Примерно в ½ случаев выявляется ТИН с ИК-депозитами
- Местный (тканевой) адаптивный иммунитет
- Преимущественно, В-лимфоциты и плазматические клетки
- Преимущественно, IgG/C3/C1q
- ГН и ТИН развиваются независимо друг от друга, но, тем не менее, ТИН крайне редко развивается изолированно (в отсутствие ГН)
- Умеренное и выраженное тубуло-интерстициальное воспаление – сильный предиктор развития тХПН
- Степень выраженности тубуло-интерстициального воспаления с позиции прогноза более важна, чем степень активности гломерулонефрита

✓ *D'Agati VD, Stokes MB. Renal disease in SLE, MCTD, Sjogren's syndrome, and RA. In Jennette JC et al.: Heptinstall's pathology of the kidney. 7th ed. 2014; 570-572.*

✓ *Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the ISN/RPS classification for lupus nephritis. Kidney International. 2018; 93(4): 789-796.*

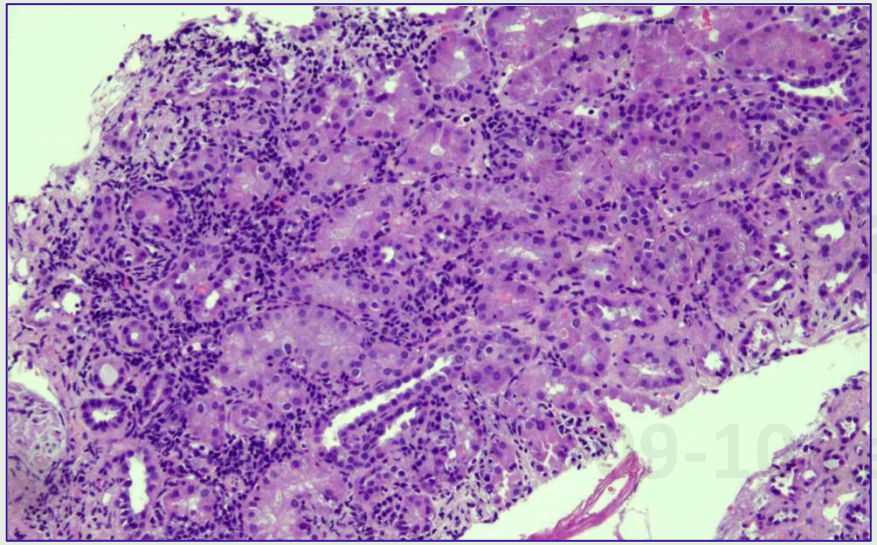


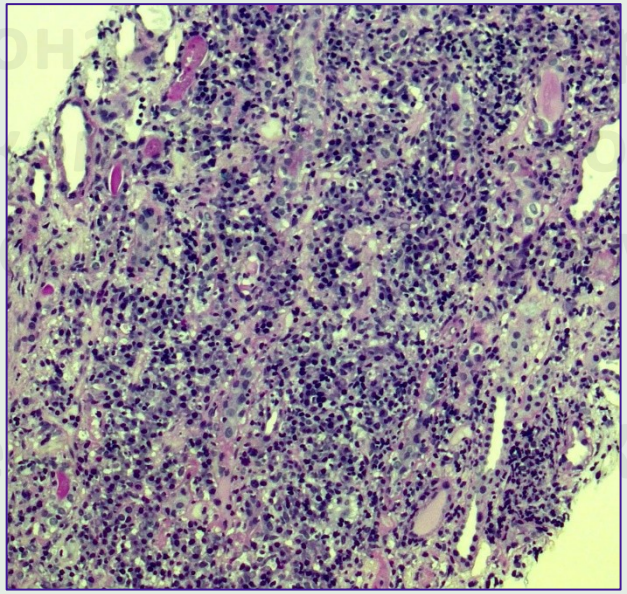


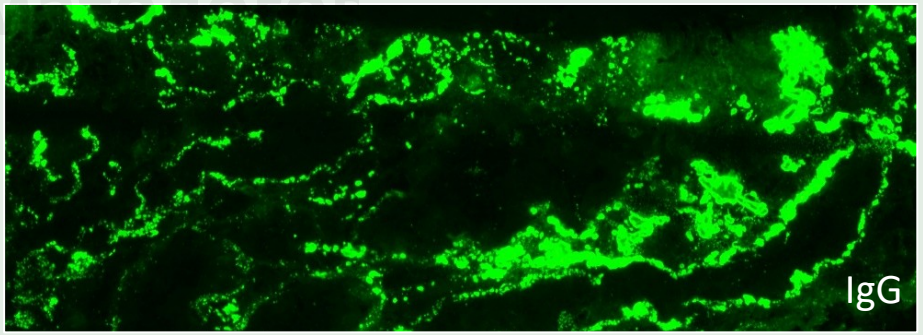


H&E, x100

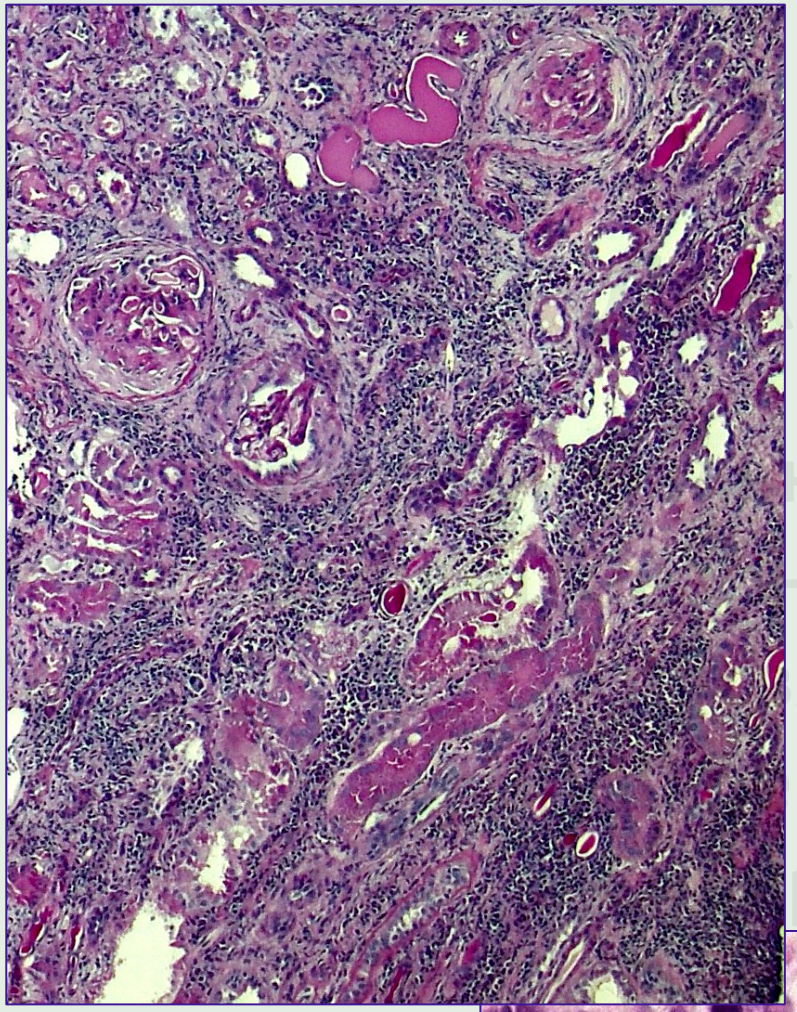
PAS, x100



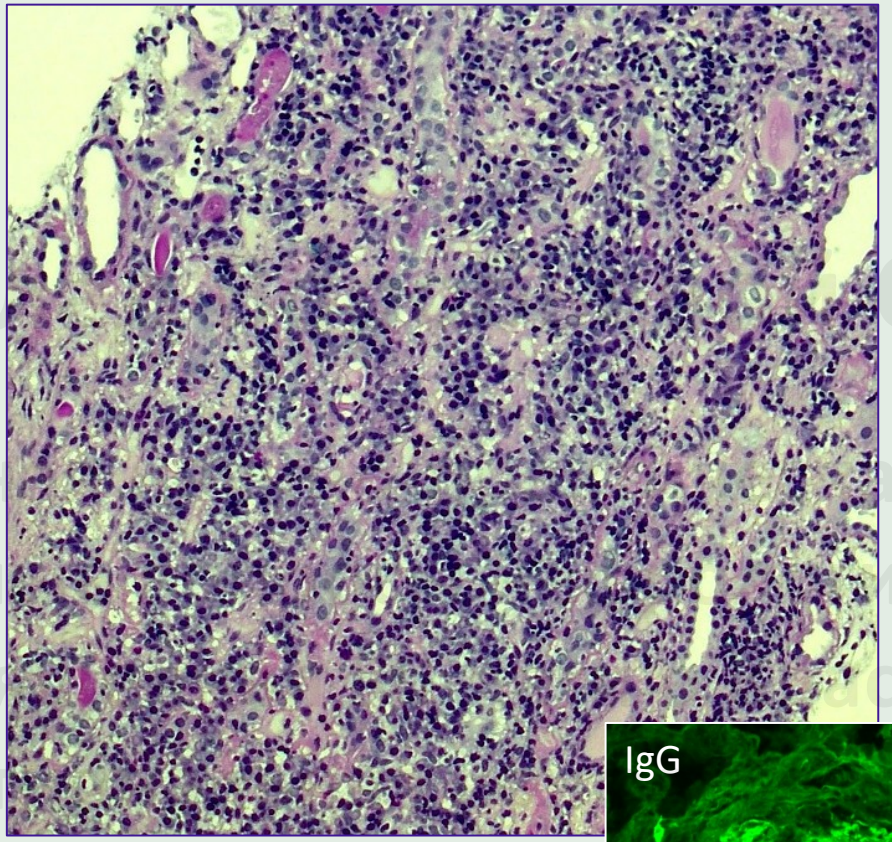




Из личного архива Воробьевой О.А., ООО «НЦКМД»



PAS, x40



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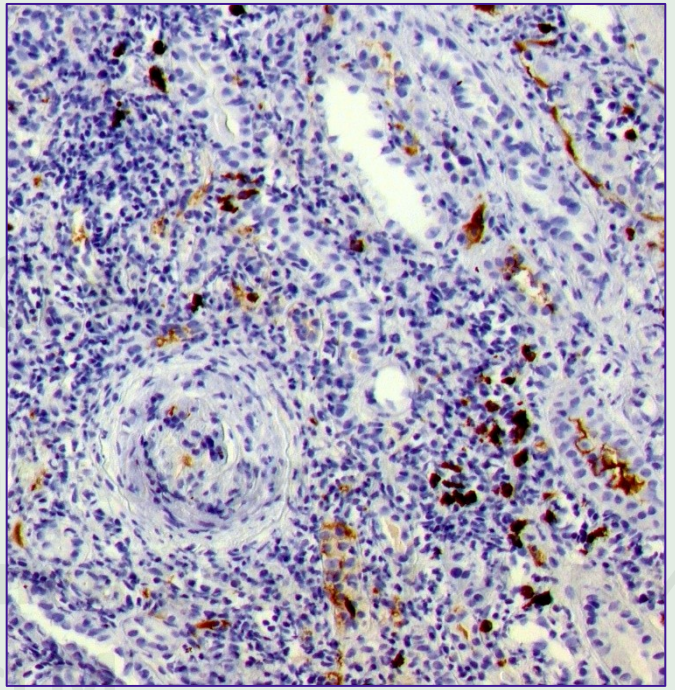
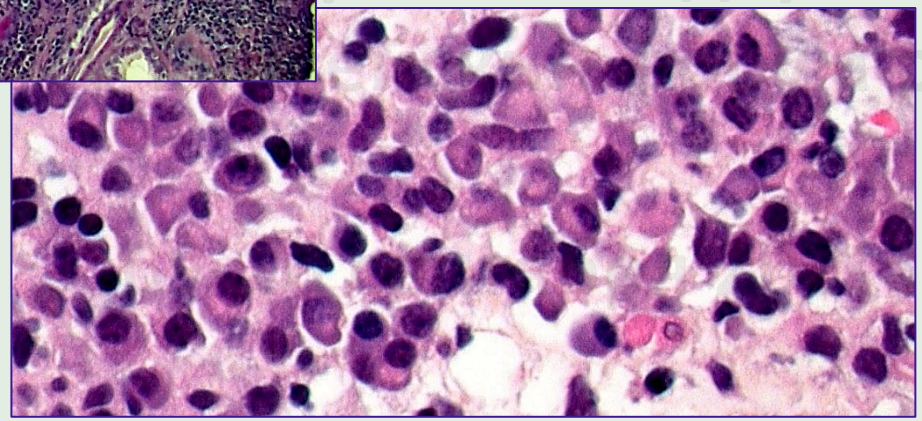
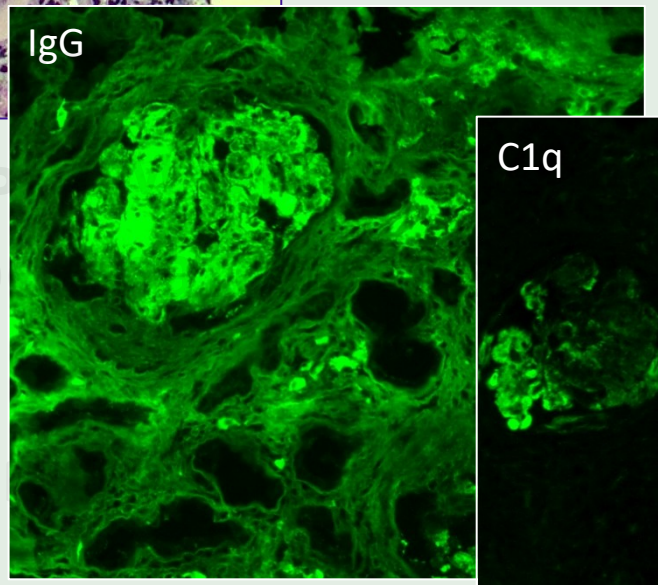
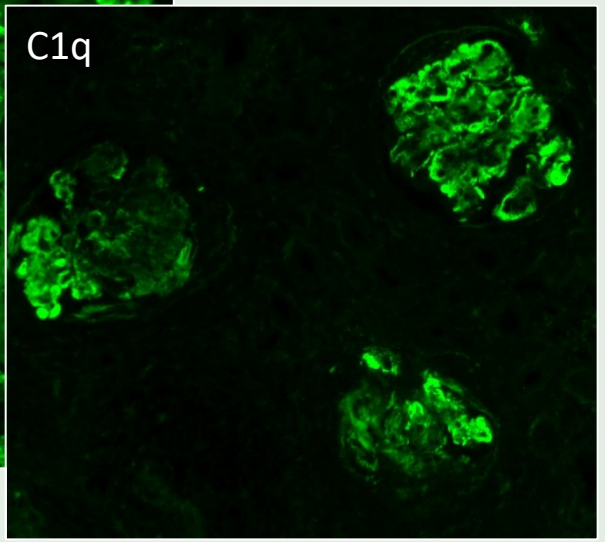


IgG4

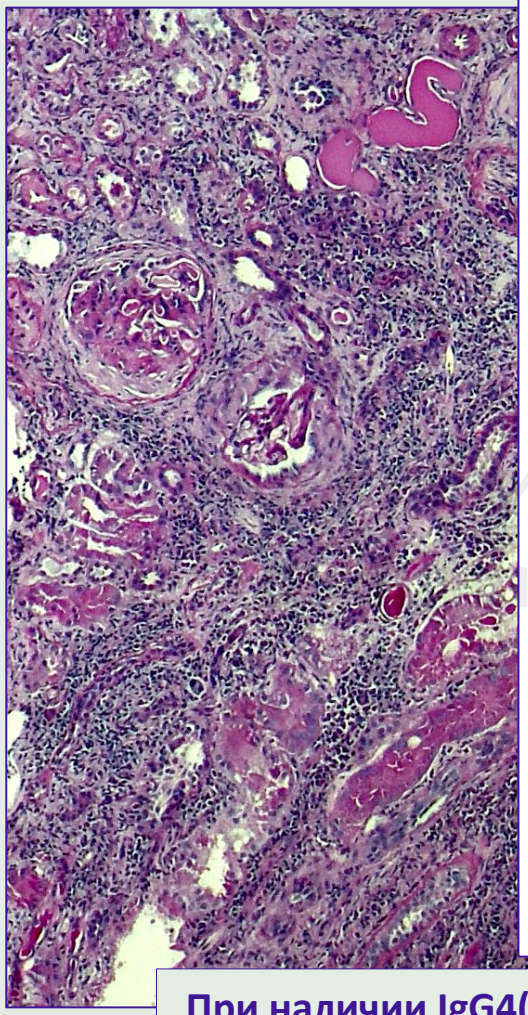


H&E, x400





Из личного архива Воробьевой О.А., ООО «НЦКМД»



PAS, x40

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http://dx.doi.org/10.4132/jptm.2015.11.09

REVIEW

Overview of IgG4-Related Tubulointerstitial Nephritis and Its Mimickers

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Beom Jin Lim

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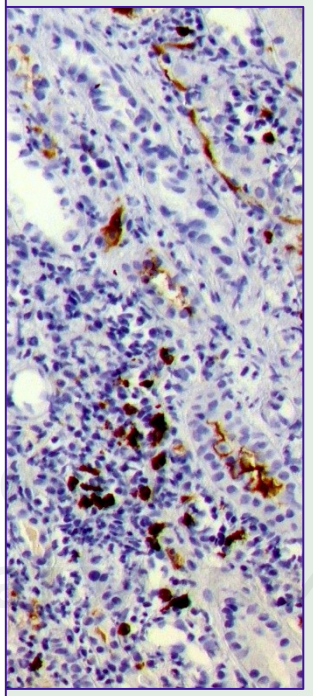
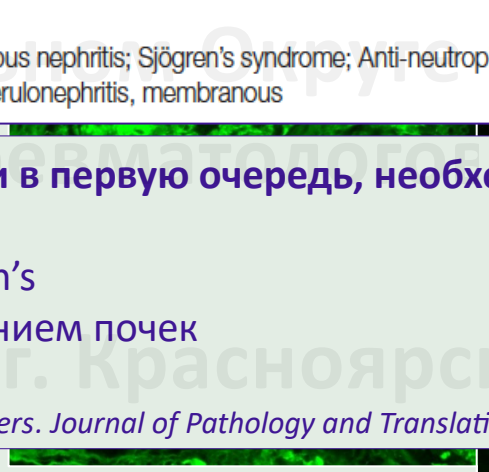
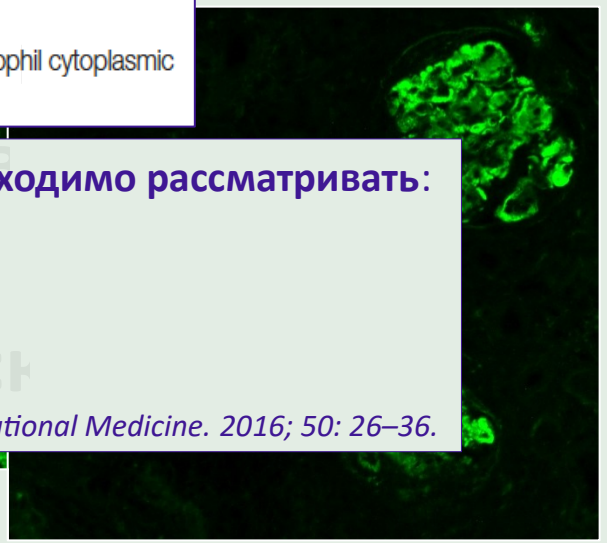
Tubulointerstitial nephritis (TIN) is the most common form of renal involvement in IgG4-related disease. It is characterized by a dominant infiltrate of IgG4-positive plasma cells in the interstitium and storiform fibrosis. Demonstration of IgG4-positive plasma cells is essential for diagnosis, but the number of IgG4-positive cells and the ratio of IgG4-positive/IgG-positive plasma cells may vary from case to case and depending on the methods of tissue sampling even in the same case. IgG4-positive plasma cells can be seen in TIN associated with systemic lupus erythematosus, Sjögren syndrome, or anti-neutrophil cytoplasmic antibody–associated vasculitis, which further add diagnostic confusion and difficulties. To have a more clear view of IgG4-TIN and to delineate differential points from other TIN with IgG4-positive plasma cell infiltrates, clinical and histological features of IgG4-TIN and its mimickers were reviewed. In the rear part, cases suggesting overlap of IgG4-TIN and its mimickers and glomerulonephritis associated with IgG4-TIN were briefly described.

Key Words: IgG4-related disease; Lupus nephritis; Sjögren's syndrome; Anti-neutrophil cytoplasmic antibody-associated vasculitis; Glomerulonephritis, membranous



IgG4





При наличии IgG4(+) тубуло-интерстициального нефрита всегда, и в первую очередь, необходимо рассматривать:

- Lupus-нефрит
- Синдром Sjögren's
- ANCA-васкулит с поражением почек

✓ *Jeong HJ, Shin SJ, Lim BJ. Overview of IgG4-related tubulointerstitial nephritis and its mimickers. Journal of Pathology and Translational Medicine. 2016; 50: 26–36.*

Из личного архива Воробьевой О.А., ООО «НЦКМД»

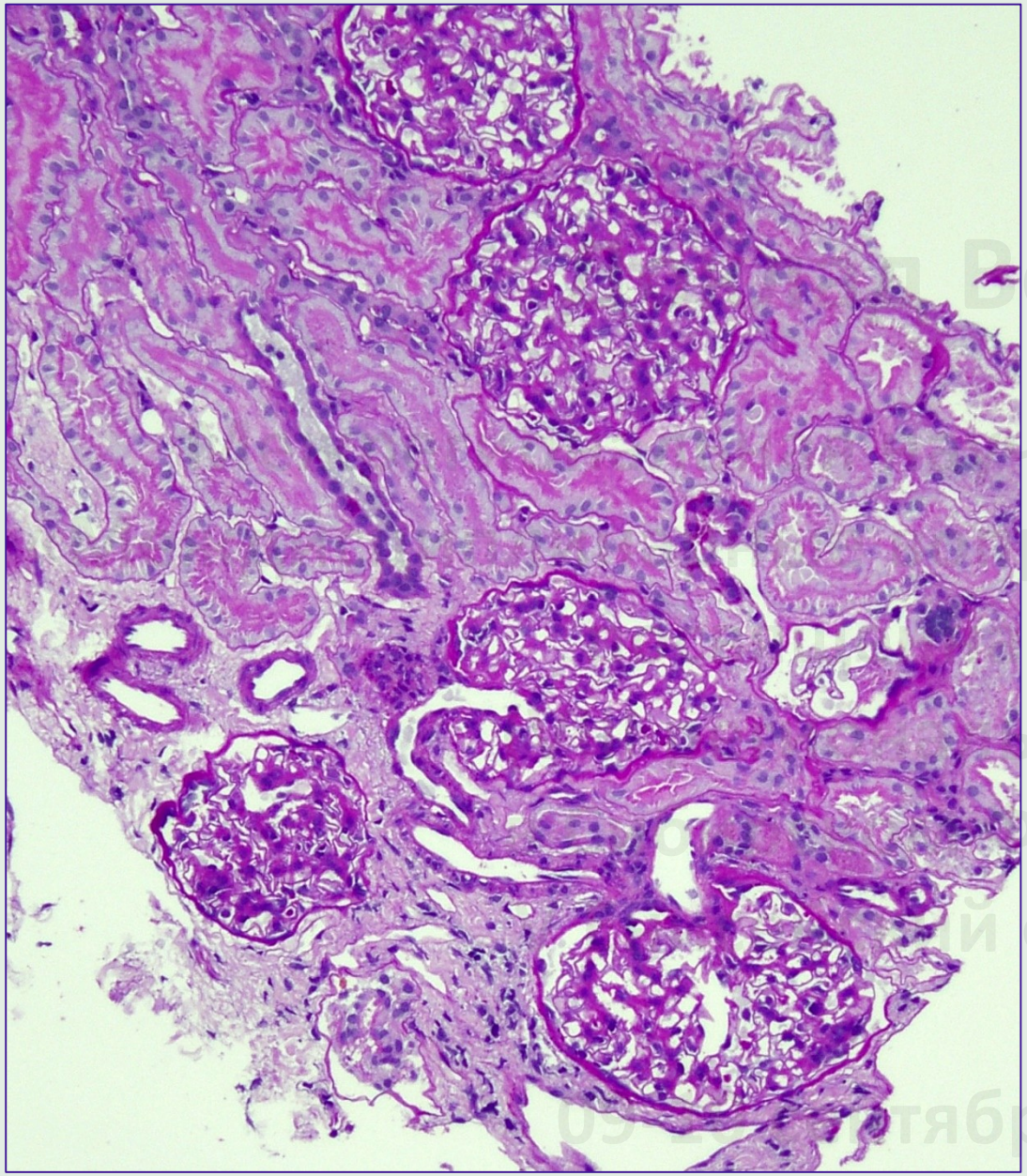
Сосудистое повреждение при СКВ

- **ИК (+)**:

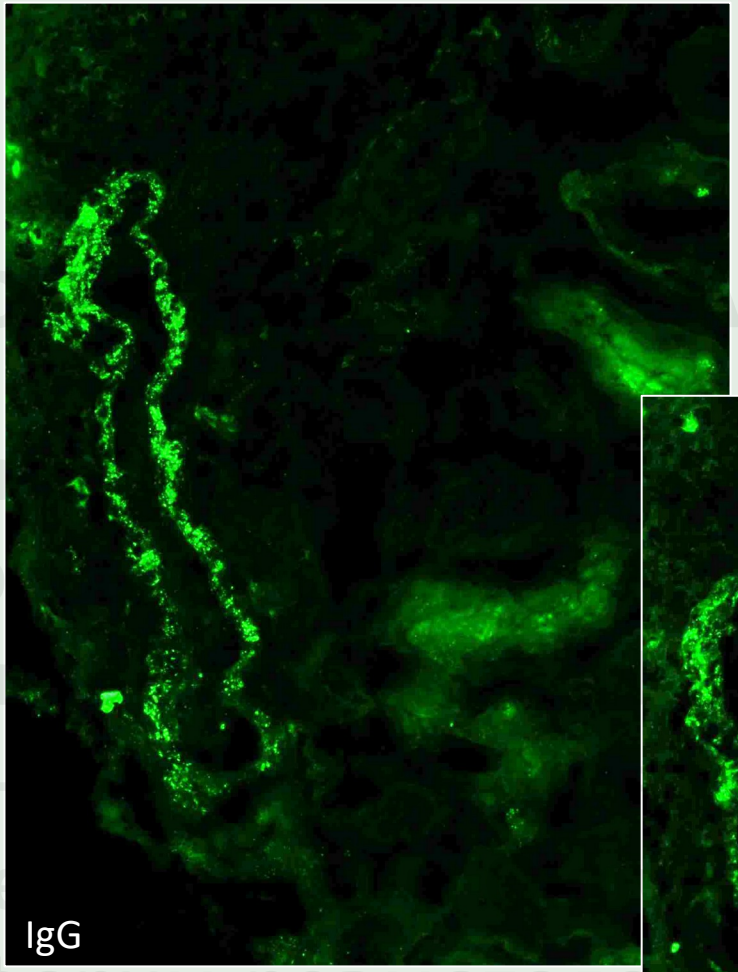
- Неосложненные иммунные комплексы (СМ – норма, ИФ – ИК-депозиты)
- Lupus-**васкулопатия** (ИК-депозиты, субэндотелиальный отек, инсудация)
- Lupus-**васкулит** (ИК-депозиты, инфильтрация, некротические изменения)

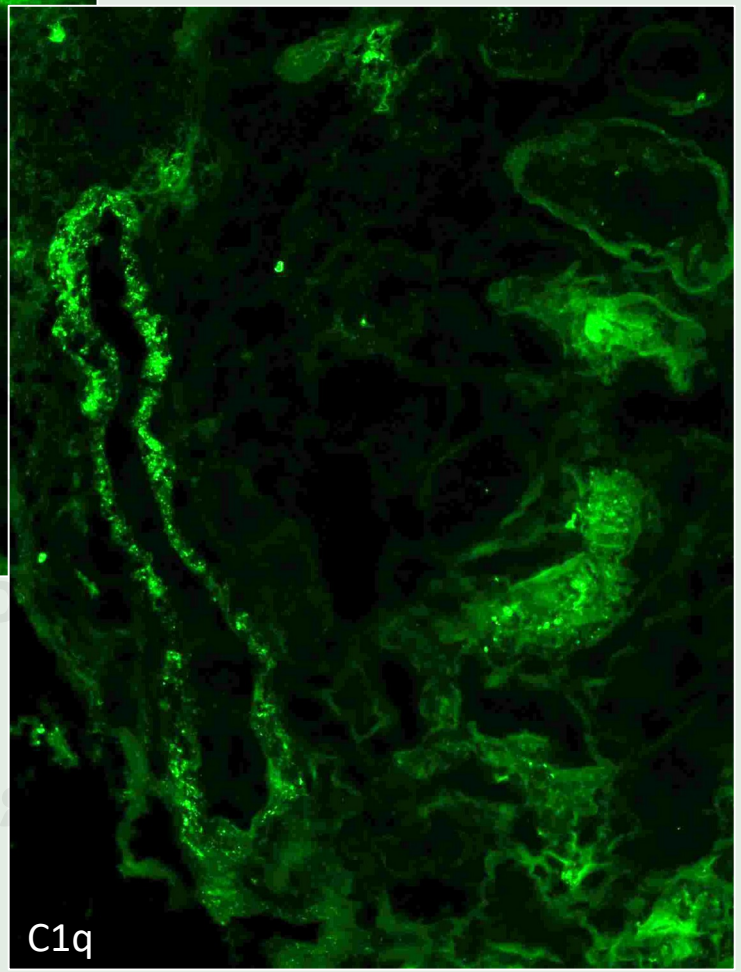
- **ИК (-)**: Гистологическая картина «**ТМА**» (в т. ч., вторичный АФС)

- Хронические фиброзно-склеротические изменения стенок сосудов



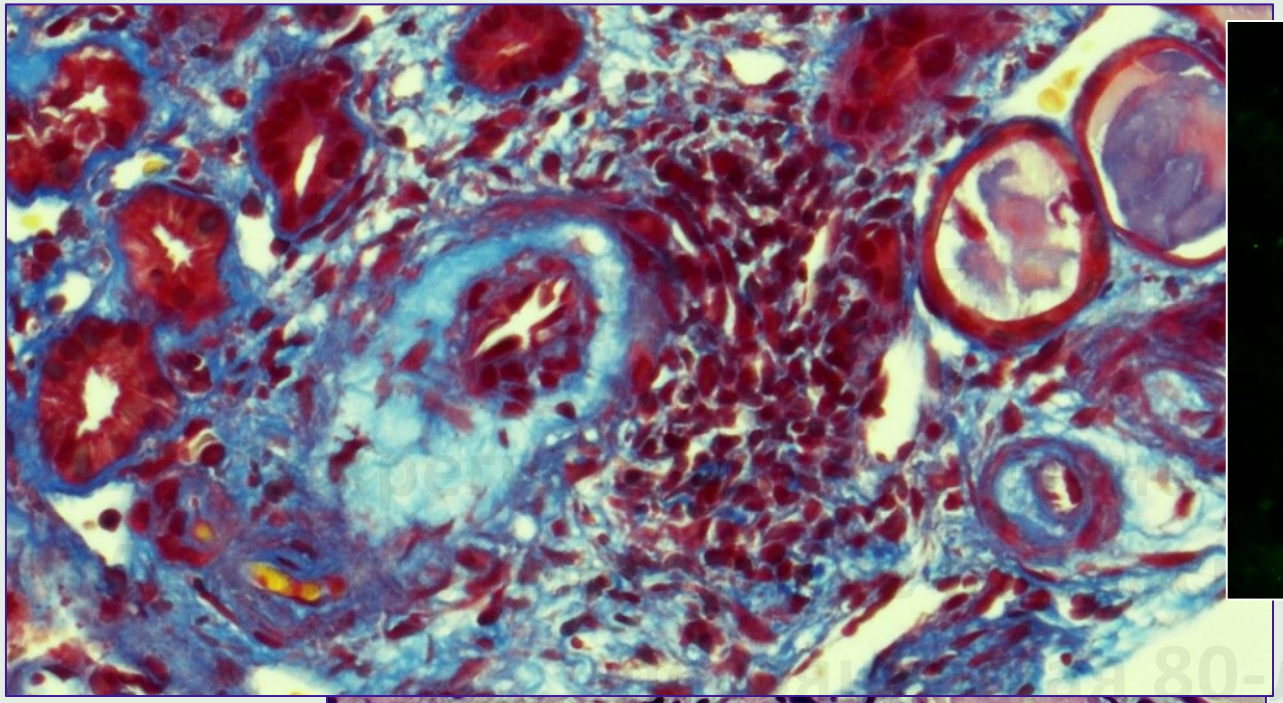
PAS, x100



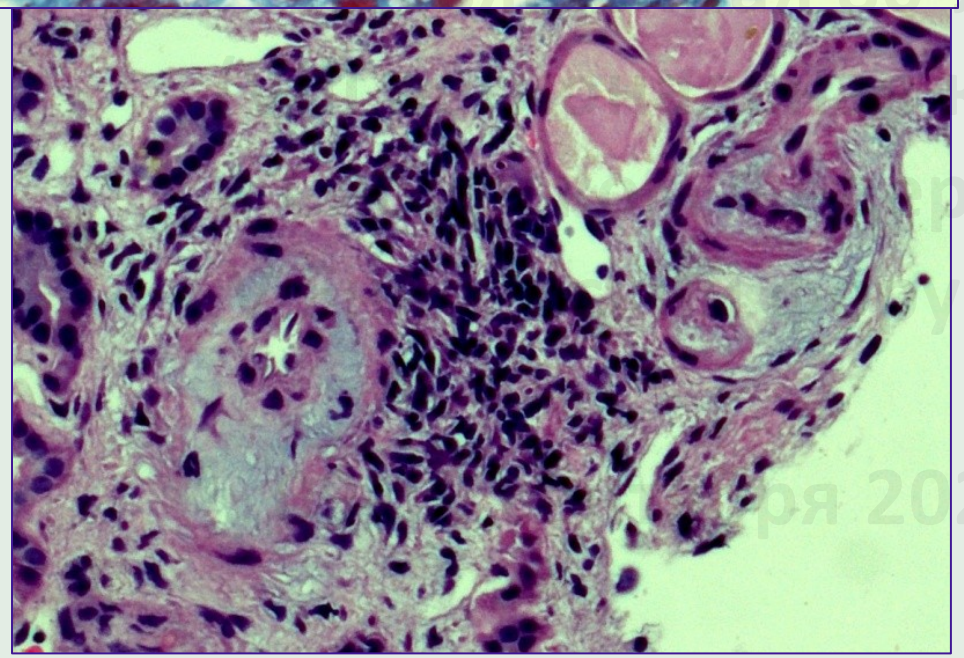


Неосложненные
иммунные комплексы

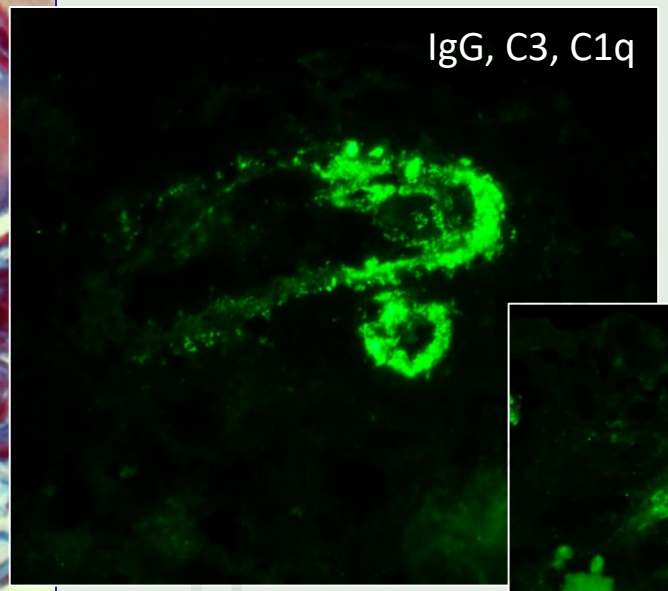
Из личного архива Воробьевой О.А., ООО «НЦКМД»

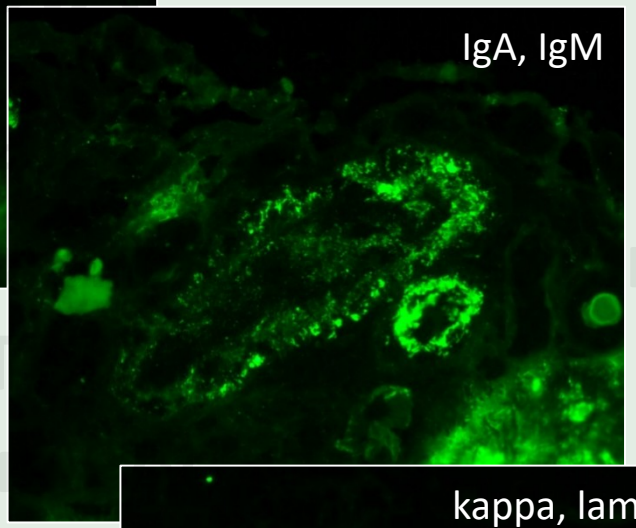


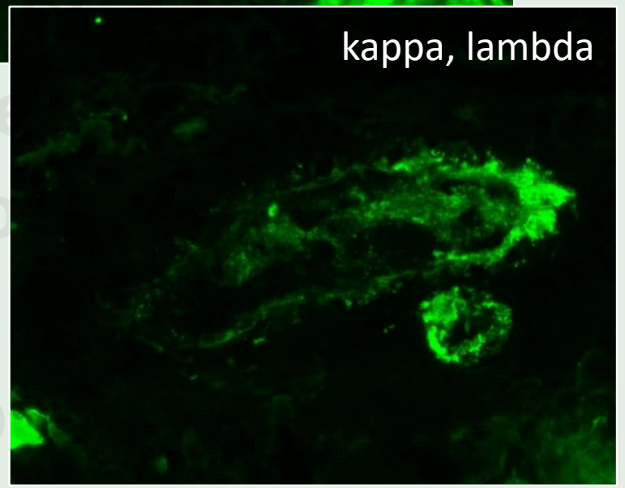
Masson’s, x200



H&E, x200



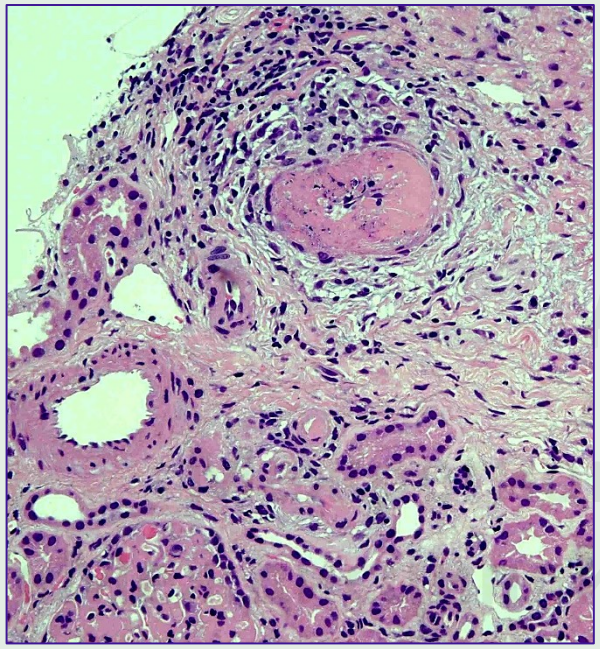




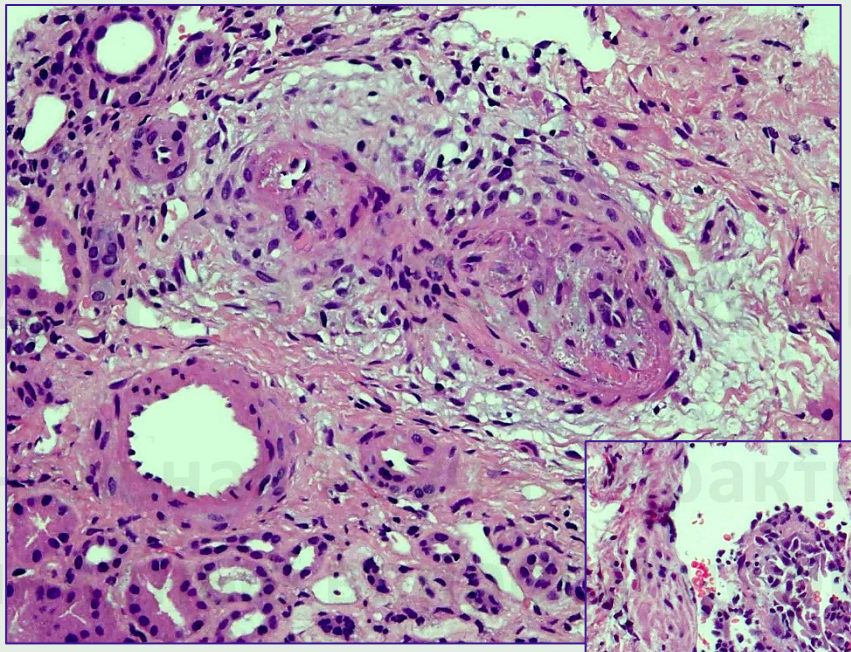
Lupus-васкулопатия

Из личного архива Воробьевой О.А., ООО «НЦКМД»

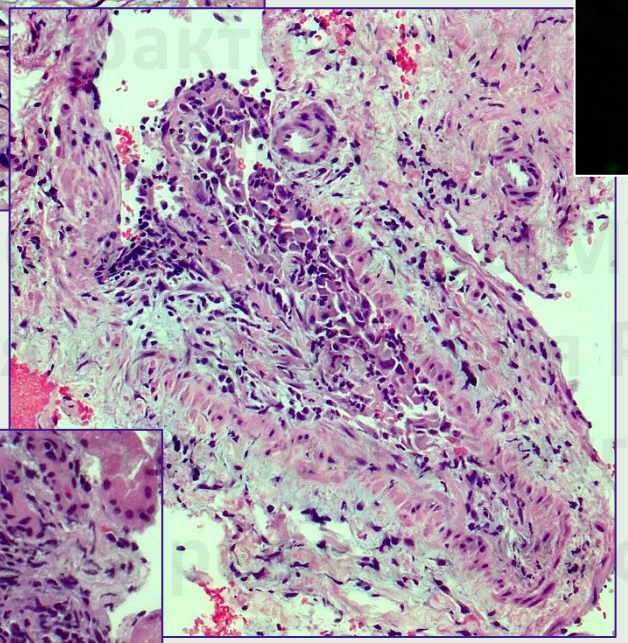
Lupus-васкулит



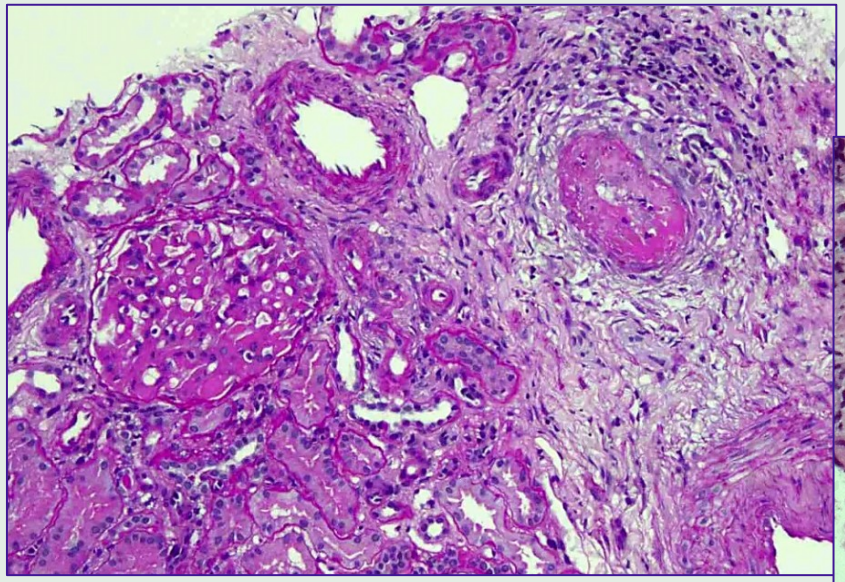
H&E, x200



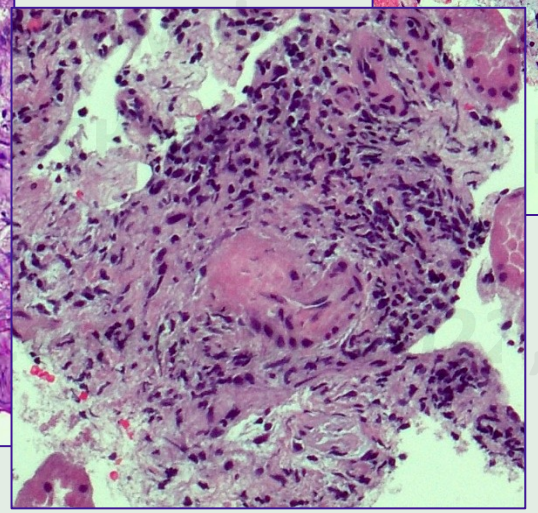
H&E, x200

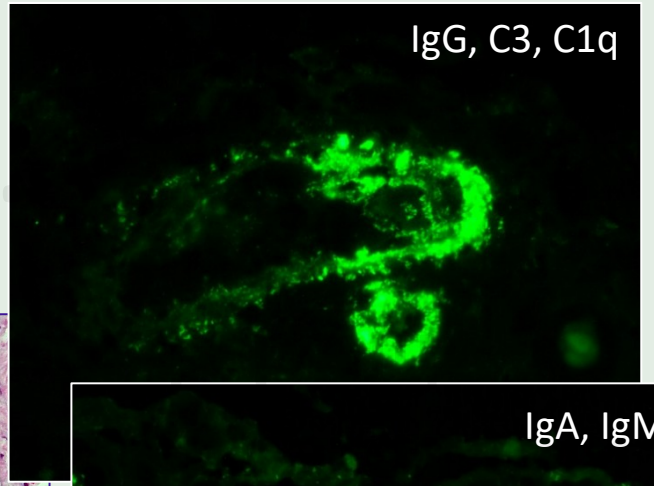


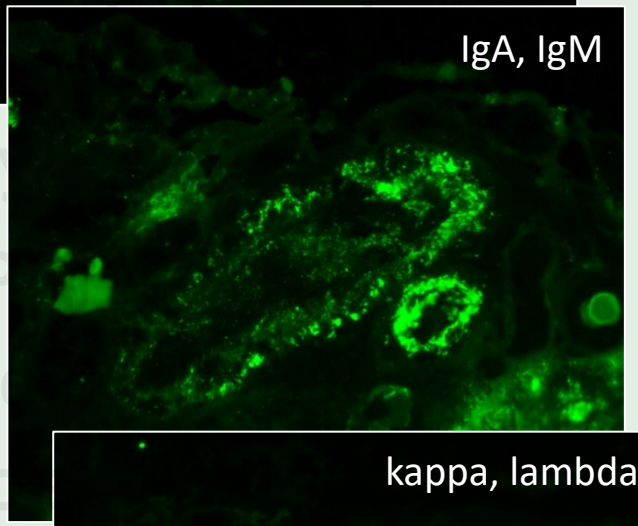
H&E, x100

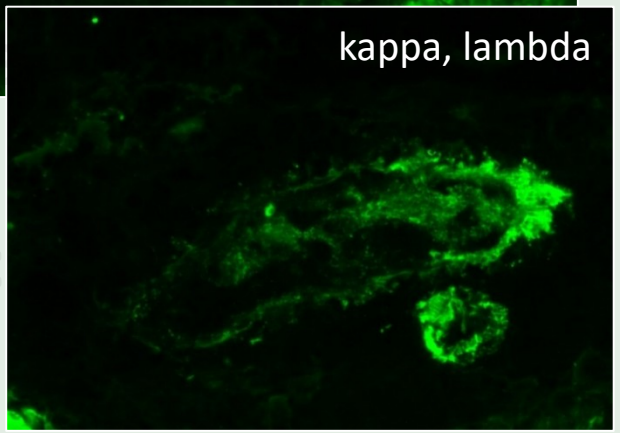


PAS, x100



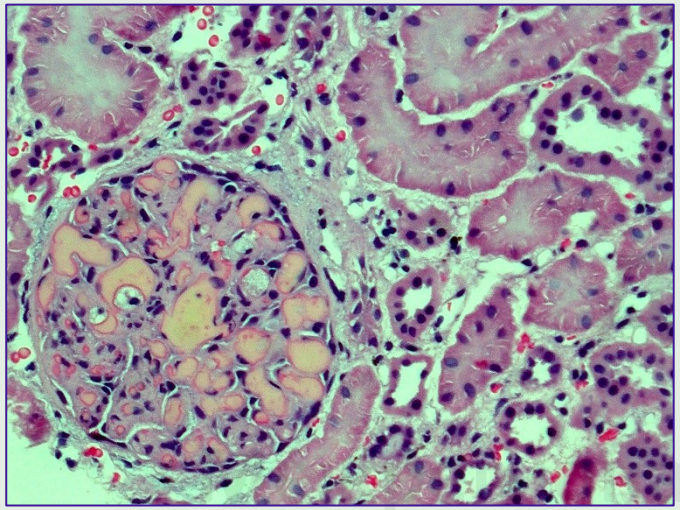


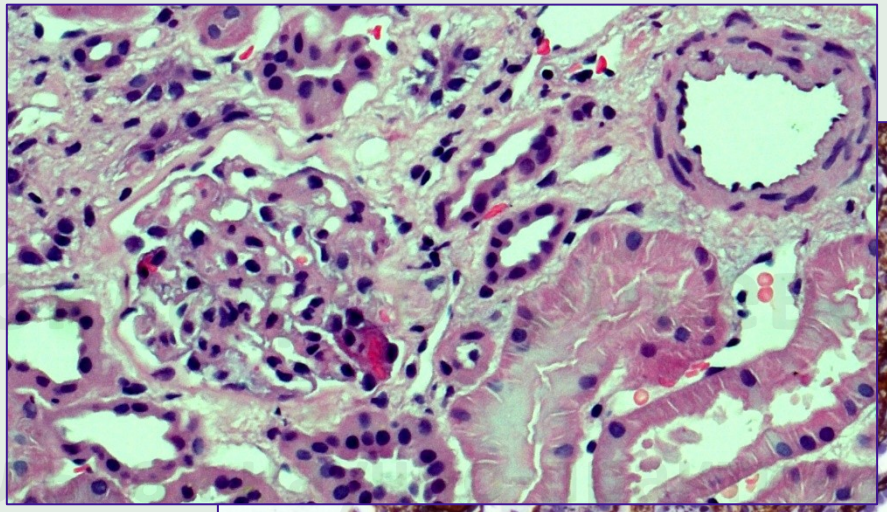




Из личного архива Воробьевой О.А., ООО «НЦКМД»

Lupus-«TMA»





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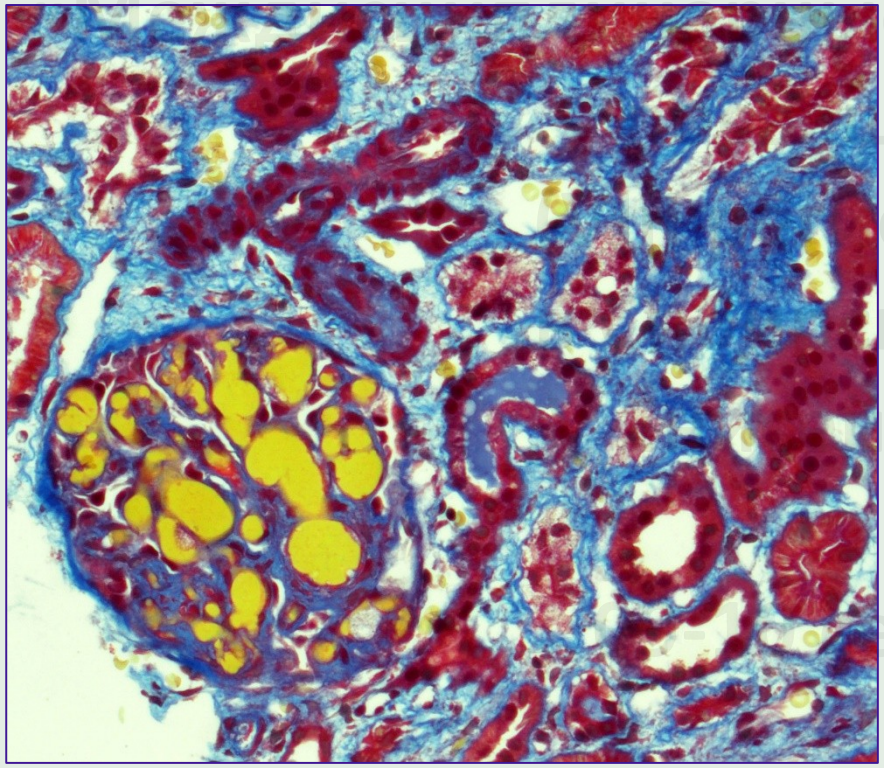
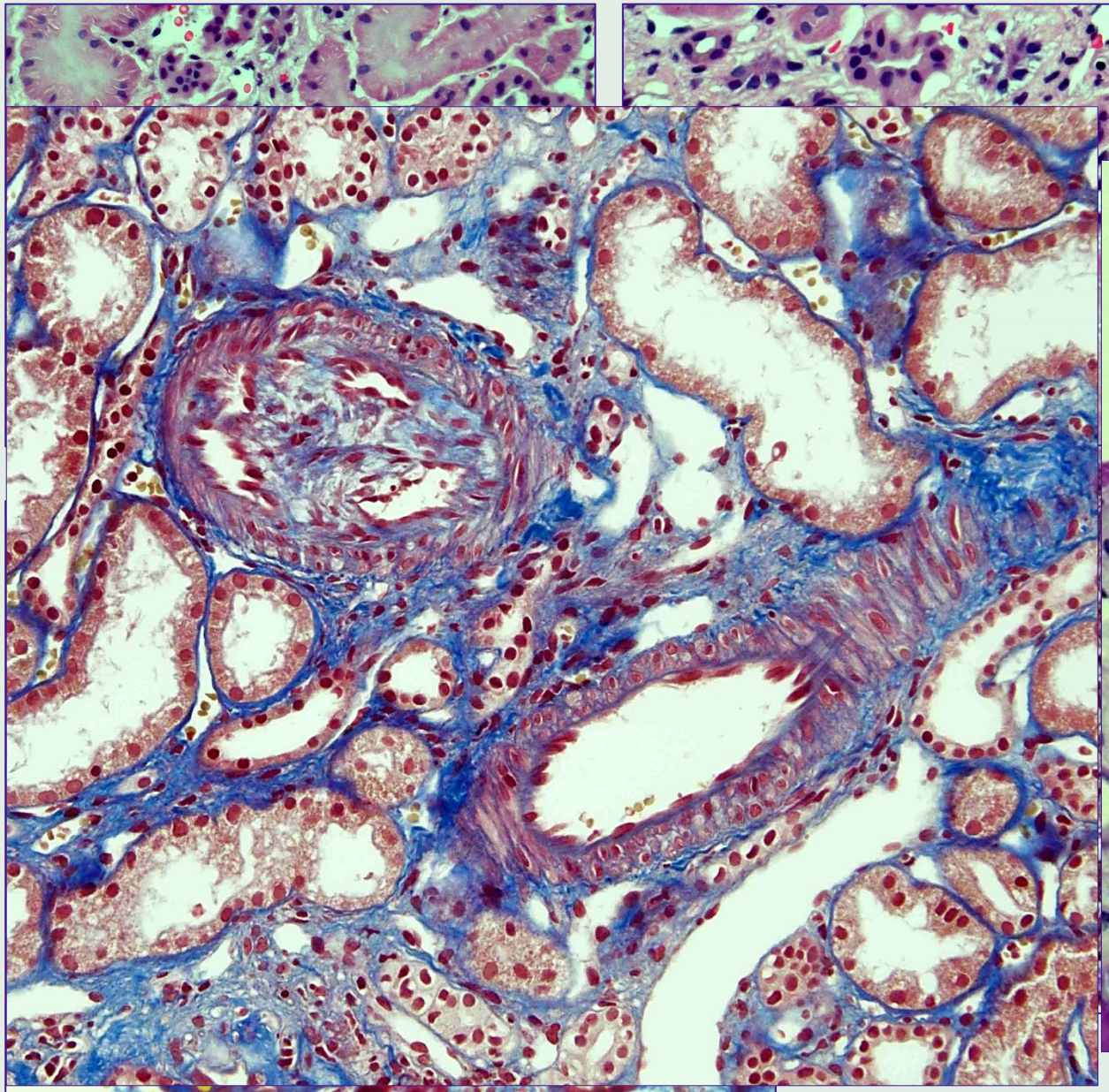


Masson’s, x200

Jones’, x100

Из личного архива Воробьевой О.А., ООО «НЦКМД»

Lupus-«ТМА»



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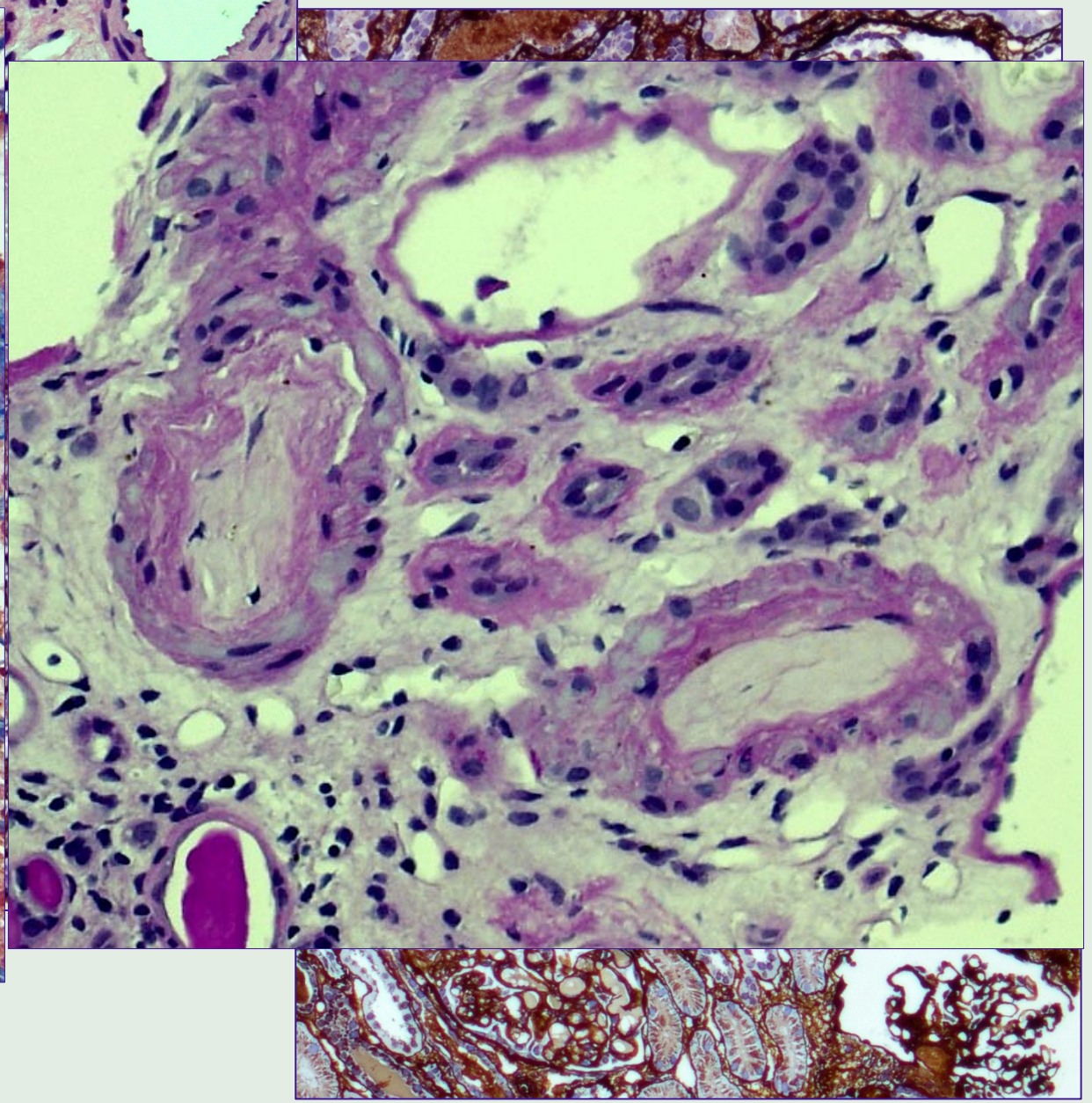


Из личного архива Воробьевой О.А., ООО «НЦКМД»

Lupus-подоцитопатия

Критерии

- Верифицированный диагноз СКВ
- Полный нефротический синдром
- Гистологическая картина БМИ или ФСГС; +/- незначительная мезангиальная гиперклеточность
- Доказанное отсутствие субэндо- и субэпителиальных депозитов (СМ, ИФ, ЭМ)
- Ультраструктурно – диффузное распластывание малых отростков подоцитов

D'Agati VD, Stokes MB. Renal disease in SLE, MCTD, Sjogren's syndrome, and RA. In Jennette JC et al.: Heptinstall's Path of the kidney. 7th ed. 2014; 609-610.

Sakhi H, Moktefi A, Bouachi K, et al. Podocyte injury in Lupus nephritis. Review. Journal Clinical Medicine. 2019, 8, 1340; doi:10.3390/jcm8091340

Olivia-Damaso N, Payan J, Oliva-Damaso E, et al. Lupus podocytopathy: an overview. Adv Chronic Kidney Dis. 2019; 26(5): 369-375.

2000-2013 гг / 3'750 Bx / 50 LP (1,33%):

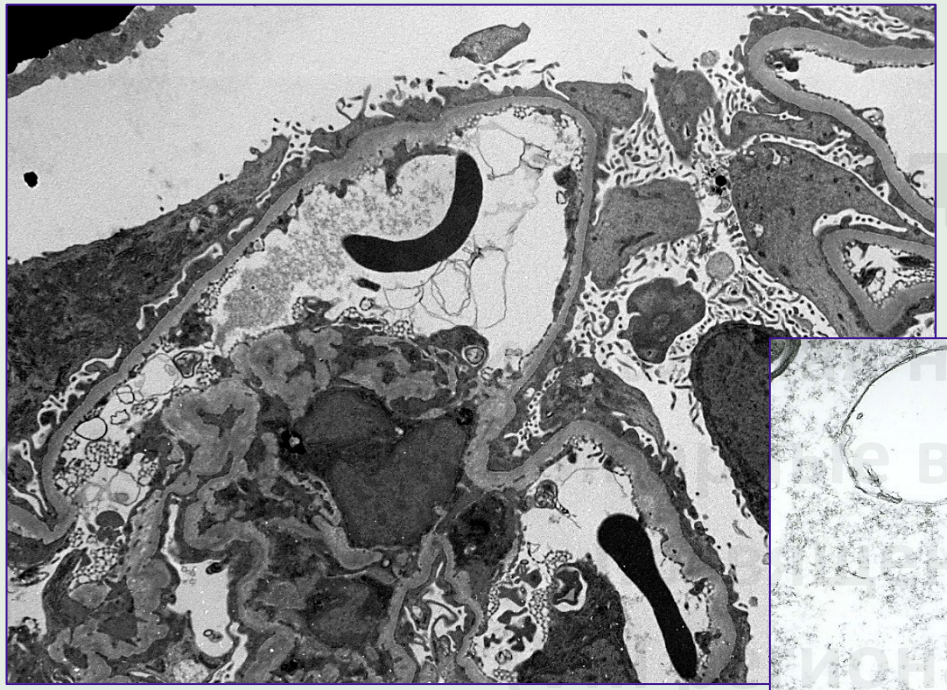
13 (≈25%) – «БМИ», М(-); 37 – М(+), в том числе 9 (≈20%) – «ФСГС»

Диффузное распластывание малых отростков подоцитов (>80%)

100% внепочечные проявления СКВ

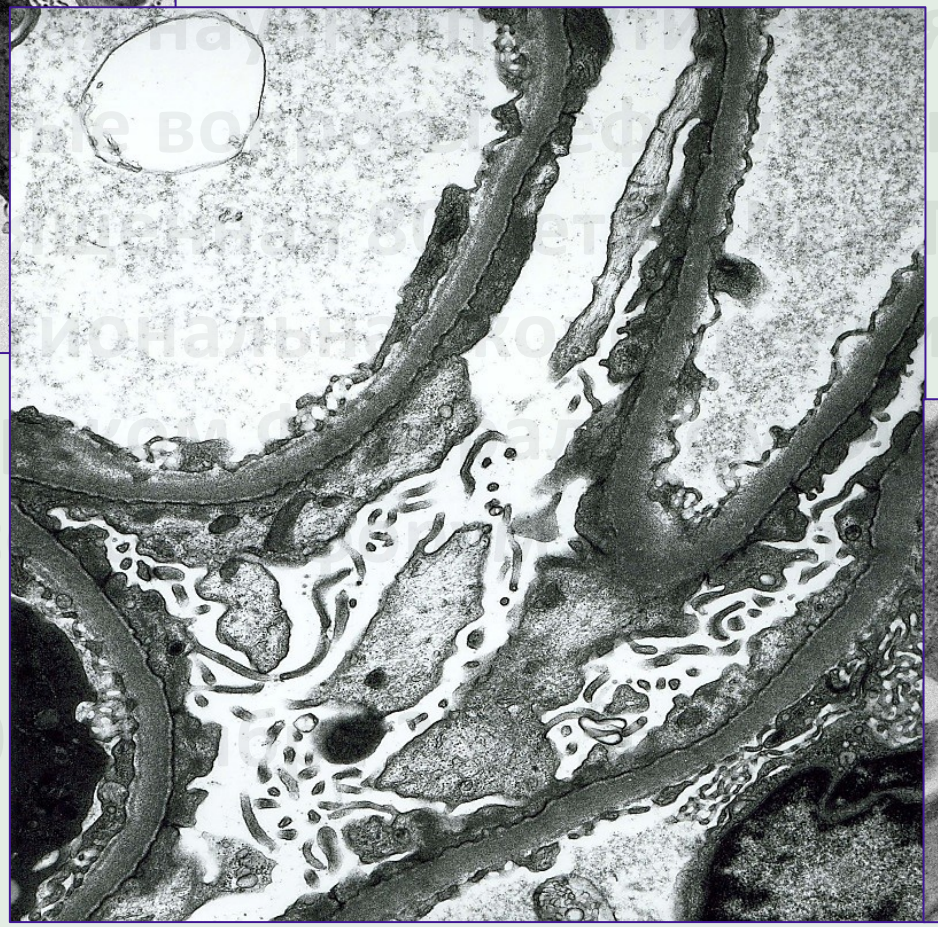
✓ *Hu W, Chen Y, Wang S, et al. Clinical-Morphological features and outcomes of lupus podocytopathy. Clin J Am Soc Nephrol. 2016 Apr 7; 11(4): 585–592.*

Lupus-подоцитопатия

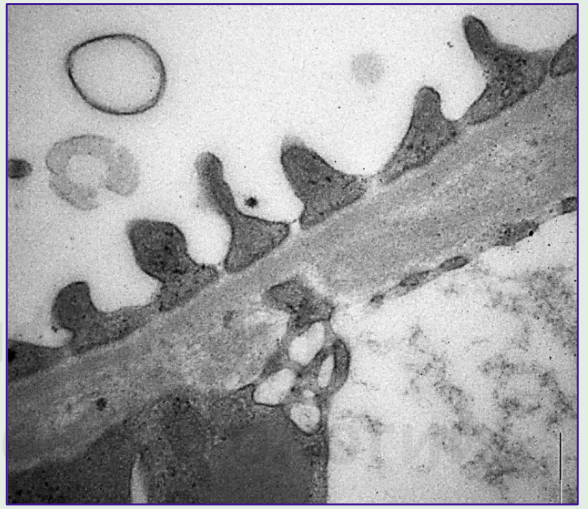


x3K

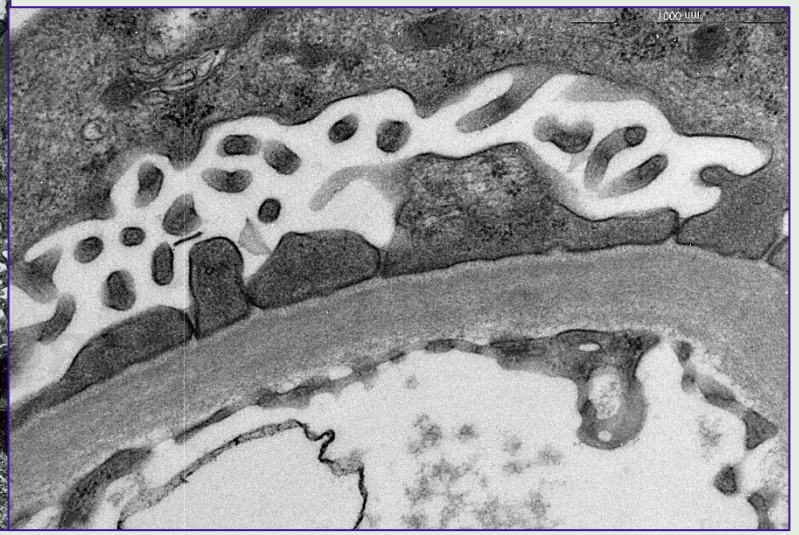
x5K



НОРМА

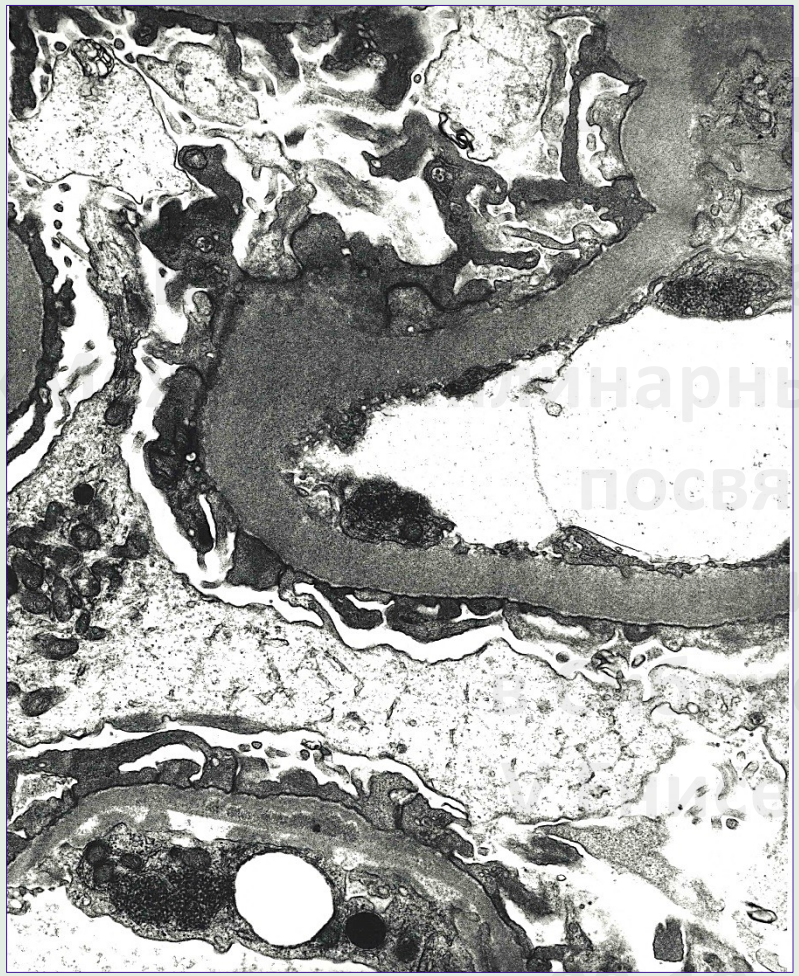


x7,5K



Из личного архива Воробьевой О.А., ООО «НЦКМД»

Тубуло-ретикулярные структуры



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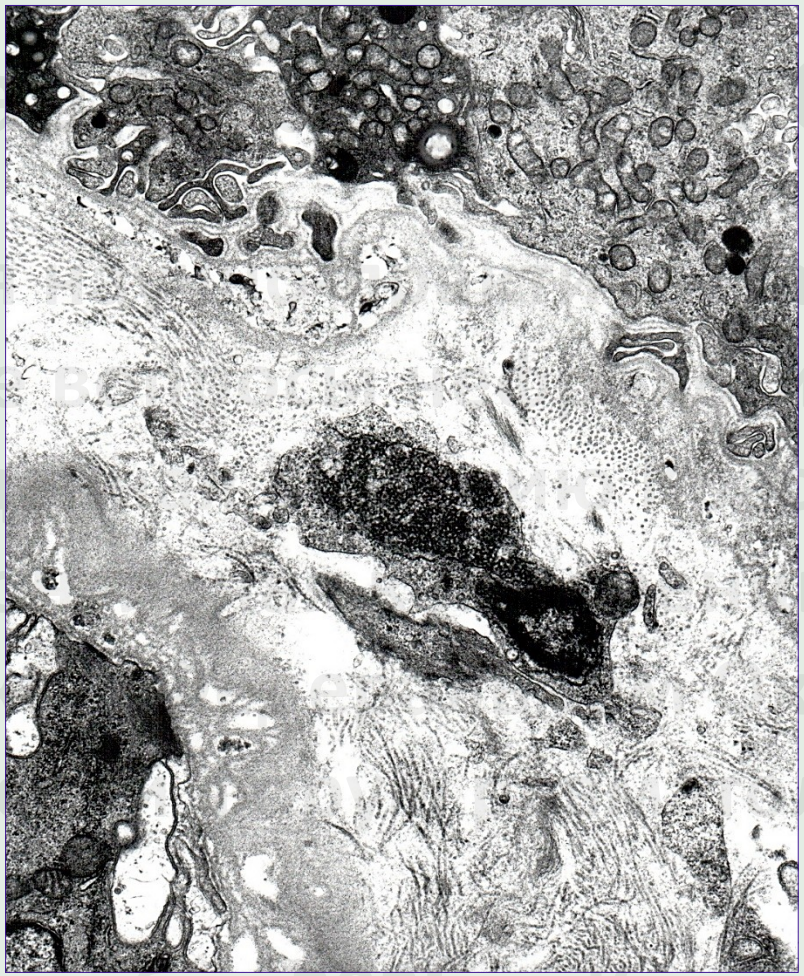

x7,5K

Не являются специфичными

Основные состояния:

- **СКВ**
- **HIV-инфекция**
- **Интерферон**

Из личного архива Воробьевой О.А., ООО «НЦКМД»

American College of Rheumatology
Empowering Rheumatology Professionals

Arthritis & Rheumatology
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DOI 10.1002/art.40930

SPECIAL ARTICLE

2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus

Martin Aringer,[1] Karen Costenbader,[2] David Daikh,[3] Ralph Brinks,[4] Marta Mosca,[5] Rosalind Ramsey-Goldman,[6] Josef S. Smolen,[7] David Wofsy,[8] Dimitrios T. Boumpas,[9] Diane L. Kamen,[10] David Jayne,[11] Ricard Cervera,[12] Nathalie Costedoat-Chalumeau,[13] Betty Diamond,[14] Dafna D. Gladman,[15] Bevra Hahn,[16] Falk Hiepe,[17] Søren Jacobsen,[18] Dinesh Khanna,[19] Kirsten Lerstrøm,[20] Elena Massarotti,[2] Joseph McCune,[21] Guillermo Ruiz-Irastorza,[22] Jorge Sanchez-Guerrero,[23] Matthias Schneider,[24] Murray Urowitz,[25] George Bertsias,[26] Bimba F. Hoyer,[27] Nicolai Leuchten,[1] Chiara Tani,[28] Sara K. Tedeschi,[2] Zahi Touma,[15] Gabriela Schmajuk,[3] Branimir Anic,[29] Florence Assan,[30] Tak Mao Chan,[31] Ann Elaine Clarke,[32] Mary K. Crow,[33] László Czirják,[34] Andrea Doria,[35] Winfried Graninger,[36] Bernadett Halda-Kiss,[34] Sarfaraz Hasni,[37] Peter M. Izmirly,[38] Michelle Jung,[32] Gábor Kumánovics,[34] Xavier Mariette,[39] Ivan Padjen,[29] José M. Pego-Reigosa,[40] Juanita Romero-Diaz,[41] Íñigo Rúa-Figueroa Fernández,[42] Raphaèle Seror,[30] Georg H. Stummvoll,[43] Yoshiya Tanaka,[44] Maria G. Tektonidou,[45] Carlos Vasconcelos,[46] Edward M. Vital,[47] Daniel J. Wallace,[48] Sule Yavuz,[49] Pier Luigi Meroni,[50] Marvin J. Fritzler,[32] Ray Naden,[51] Thomas Dörner,[17] and Sindhu R. Johnson[52]

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Ray Naden,[51] Thomas Dörn...

Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR	
Anti-Smith antibody	6

Total score:

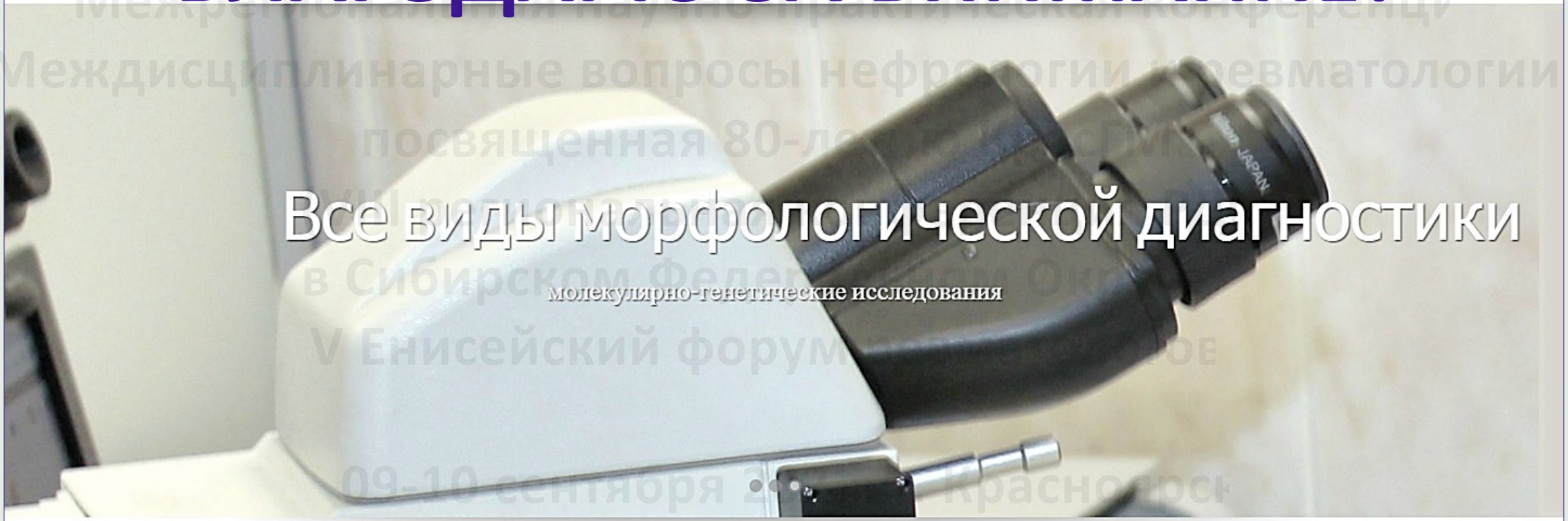
↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

НАЦИОНАЛЬНЫЙ ЦЕНТР
КЛИНИЧЕСКОЙ МОРФОЛОГИЧЕСКОЙ ДИАГНОСТИКИ

Доклад Воробьевой О.А

БЛАГОДАРЮ ЗА ВНИМАНИЕ!



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V Енисейский форум
09-10 сентября 2